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AMERICAN COLLEGE OF CHEST PHYSICIANS

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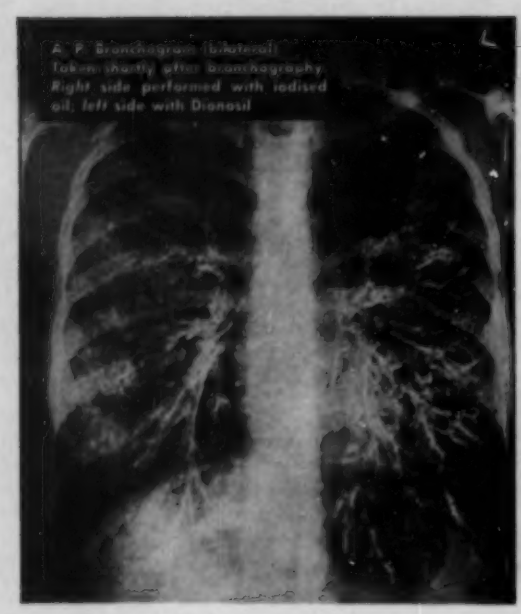

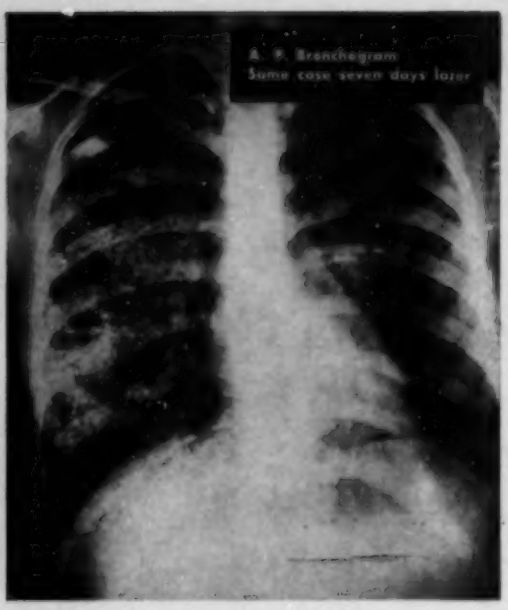

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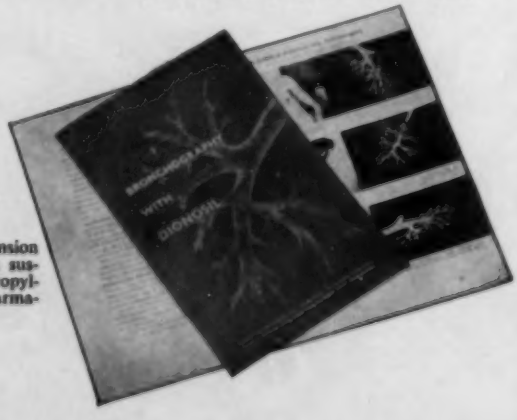

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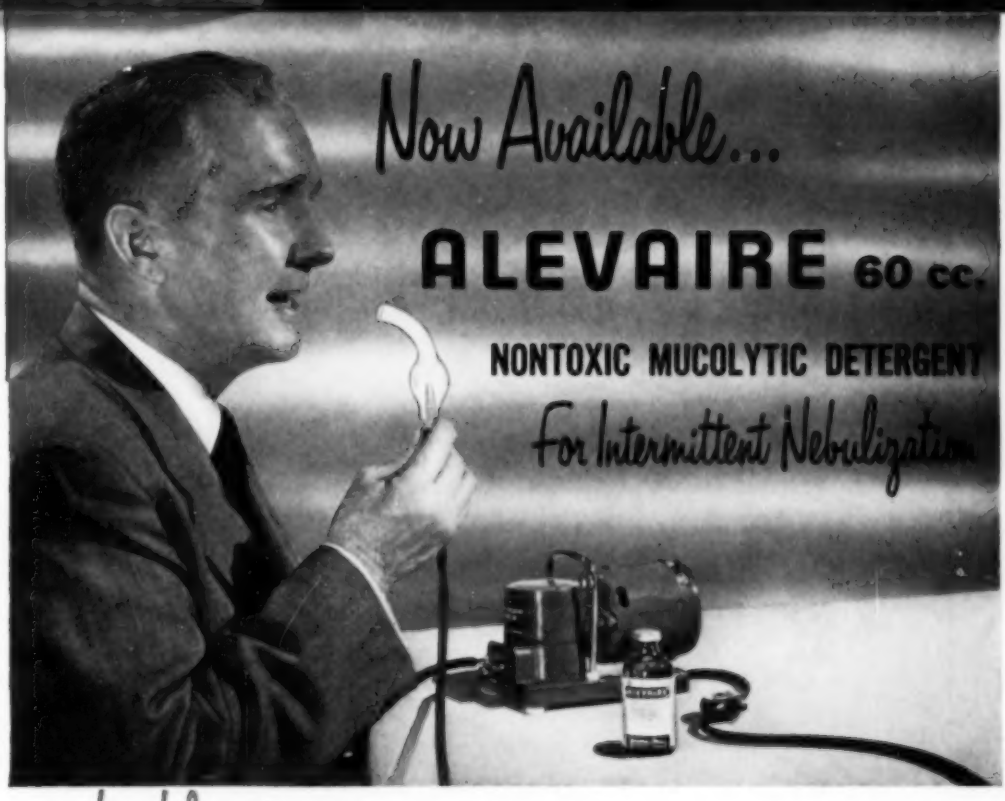

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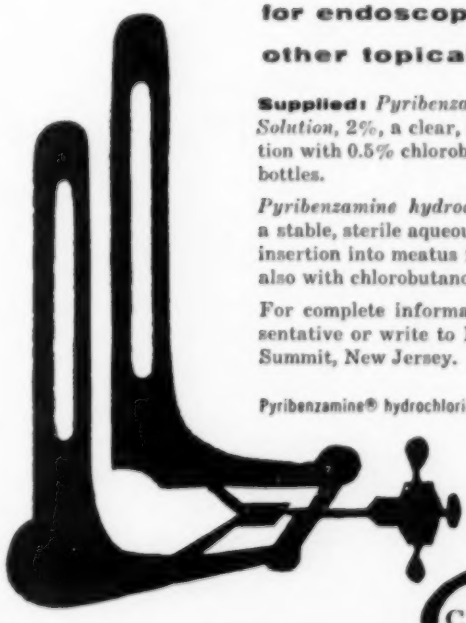

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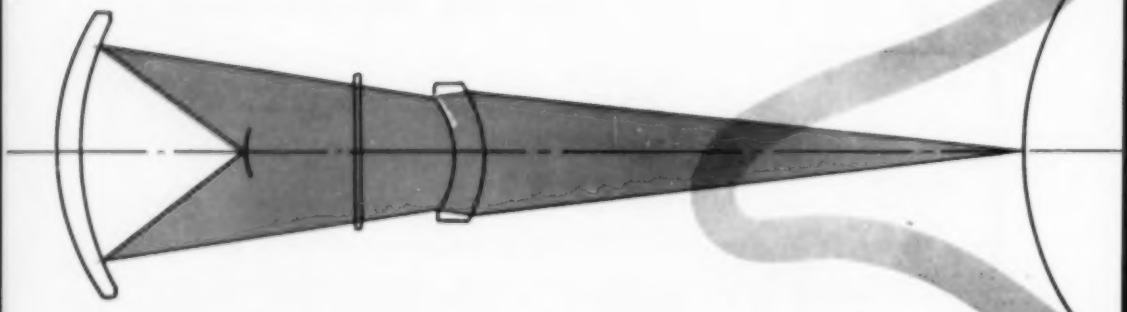

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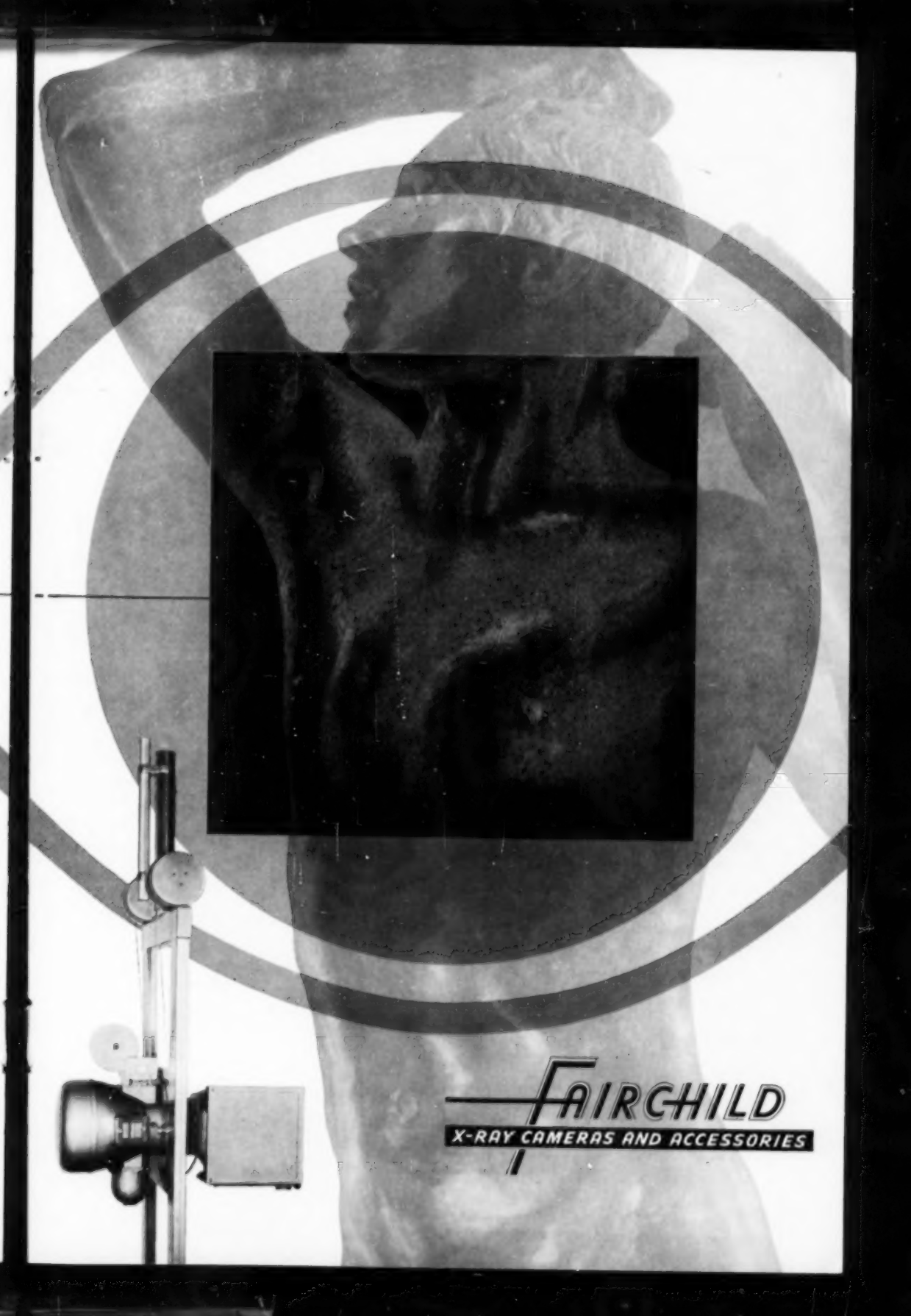
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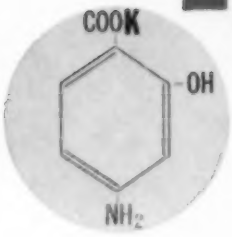

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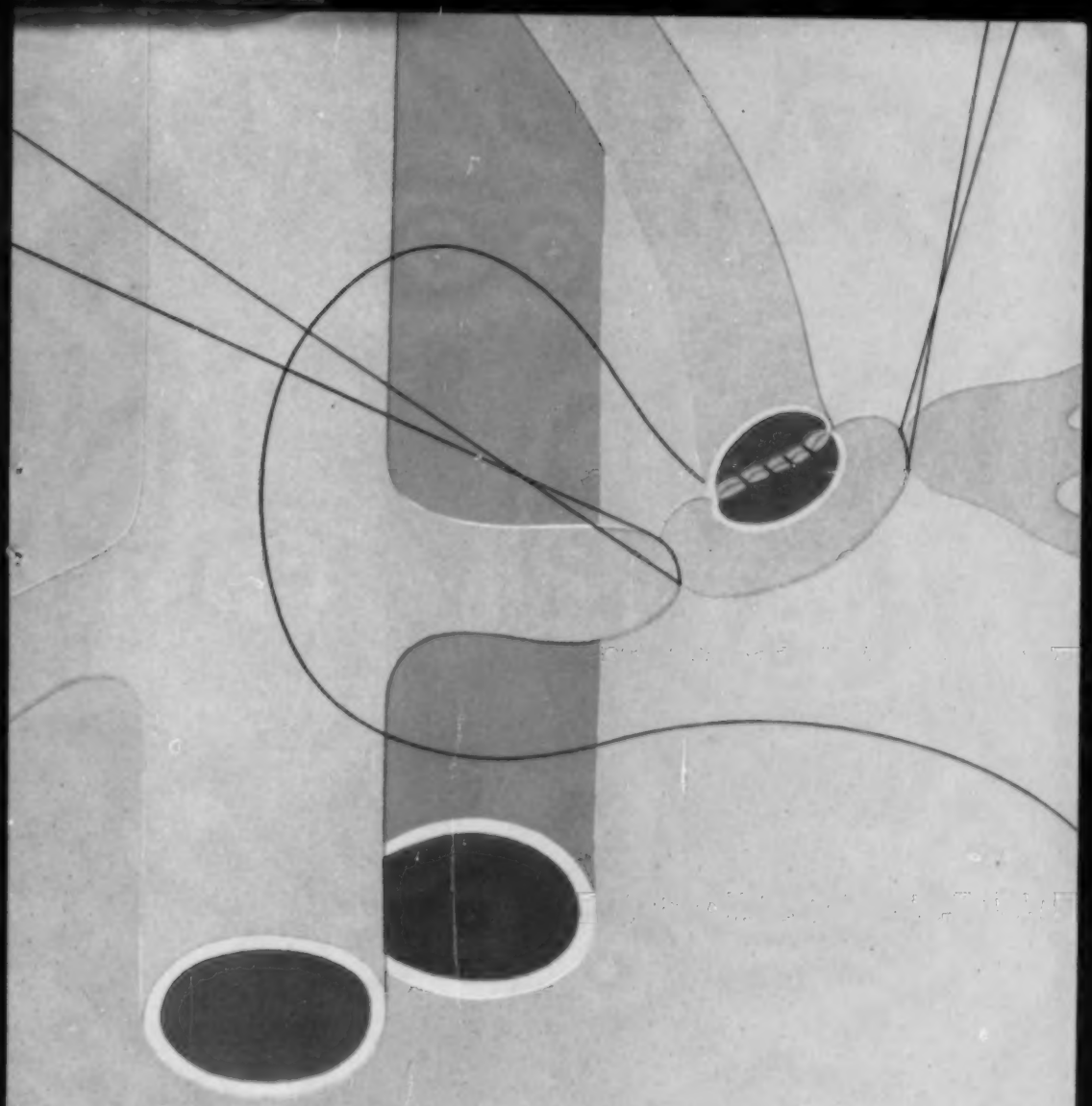

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History

The first investigation of a hemostat with an action comparable to Adrenosem Salicylate was made by Derouaux and Roskam[1] in 1937. They reported that an oxidation product of adrenalin, adrenochrome (which has no sympathomimetic properties), has prompt hemostatic activity.

It was further found that various combinations of adrenochrome, notably the oxime and semicarbazone, produced stable solutions. But, these were so slightly soluble that sufficient concentration could not be obtained for practical therapeutic use. By combining these adrenochrome compounds in a sodium salicylate complex a stable, soluble form can be obtained. This complex has been given the generic name, carbazochrome salicylate, and is supplied under the trade name Adrenosem Salicylate.

Roskam, in his study entitled "The Arrest of Bleeding,"[2] enumerates "the drugs whose efficaciousness as hemostatics have been proved by accurate methods in experimental animals and in healthy men as well. . . . One is the monosemicarbazone of adrenochrome [Adrenosem Salicylate]."

Chemistry

Adrenosem Salicylate is a synthetic chemical. The full chemical name is adrenochrome monosemicarbazone sodium salicylate complex.

Pharmacology

Although it is chemically related to epinephrine, Adrenosem Salicylate has no sympathomimetic effects. It does not alter blood components, nor does it affect blood pressure or cardiac rate.[2-7]

(* U.S. Patent 2,581,850)

Sherber, in an early study,[3] concludes that Adrenosem Salicylate* "is a potent antihemorrhagic factor in those conditions in which the integrity of the smaller vessels is interrupted, and is superior to any similar material that is now available."

He continues, "From our experience it appears that adrenochromazone complex is indicated in preventing vascular accidents incident to hypertension; in maintaining small vessel integrity; in the preoperative preparation where oozing from a vascular bed is anticipated, as in tonsillectomies, adenoidectomies and prostatectomies; and as an adjunct in the treatment of bleeding from such surgical procedures."

Adrenosem Salicylate may be administered simultaneously (but separately) with any type of anesthetic, anticoagulant, or vitamin K and heparin.

A Unique Systemic Hemostat

Clinical investigators[2-7] are in agreement that Adrenosem Salicylate controls bleeding and oozing by decreasing capillary permeability and by promoting the retraction of severed capillary ends. It aids in maintaining normal capillary integrity by direct action on the intercellular "cement" in capillary walls. The interesting work of Fulton[5] confirms this. Adrenosem Salicylate, since it is not a vasoconstrictor, has no effect on large severed blood vessels and arterioles.

Adrenosem Salicylate is being used both prophylactically and therapeutically in thousands of hospitals, and in virtually every type of surgical procedure. It has also proved most useful in dental surgery.[7]

Owings reported on the use of Adrenosem Salicylate in controlling postoperative adenoid bleeding in 102 cases.[4] "We have used 2½ mg.

(½ ampule) intramuscularly, 15 minutes before anesthesia for children and 5 mg. (1 ampule) for adults." In only one patient did bleeding occur. Three others showed red blood from the nose and mouth. These patients "were then given 5 mg. intramuscularly, with prompt and complete control. We have also noticed that bleeding stopped more promptly on the operating table."

This is a 1% incidence of postoperative bleeding using Adrenosem Salicylate preoperatively, compared to an incidence of 10% postoperative bleeding in all cases taken from previous records, without Adrenosem Salicylate medication.

Peele reports on the use of Adrenosem Salicylate in treating 178 patients with 24 different conditions.[5] The drug was first used to control postoperative hemorrhage from the adenoid region. He adds: "The results were so dramatic that since that date [1953] Adrenosem Salicylate has been used postoperatively to reduce bleeding from all otolaryngologic and bronchoesophagolic procedures, to treat postoperative hemorrhage from the tonsil and adenoid regions, and to treat selected cases of epistaxis."

The effectiveness of Adrenosem Salicylate in controlling bleeding and oozing in 330 patients is reviewed by Bacala.[6] "Our experience of the effect of carbazochrome salicylate on 317 surgical indications and 13 obstetricogynecological conditions, has been therapeutically encouraging and successful for the control of capillary bleeding. Foremost among the cases studied were 223 tonsillectomies definitely benefited by this metabolic hemostat, making a diminution of the control incidence of posttonsillectomy bleeding of 19.8% down to 7%. It has also been found useful in gastro-intestinal bleeding, cataract extraction, epistaxis, incisional seepage, trans-urethral prostatectomy, menometrorrhagias, cervical ooze, antepartum and postpartum bleeding, threatened abortion, and prevention of capillary hemorrhages during hedulin or dicumerol therapy."

Side Effects

All investigators concur that, at recommended dosage levels, Adrenosem Salicylate is free from toxic effects. No cumulative effects attributable to the drug have been reported.

The only side reaction noted has been a transient stinging sensation in the area of injection when Adrenosem Salicylate is used intramuscularly. As one investigator comments: "The brief discomfort which attends the injection of Adrenosem into the gluteal region has not been a significant problem in children or adults as originally anticipated."[5]

Indications

Idiopathic purpura, retinal hemorrhage, familial telangiectasia, epistaxis, hemoptysis, hematuria.

Postoperative bleeding associated with:
tonsillectomy, adenoidectomy and nasopharynx surgery;
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uterine bleeding;
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dental surgery;
chest surgery and chronic pulmonary bleeding.

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For recommended dosage schedules, please send for detailed literature.

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Tablets: 2.5 mg. S.C. Yellow, bottles of 50.
Syrup: 2.5 mg. per 5 cc. (1 tsp.), 4 ounce bottles.

References

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DISEASES of the CHEST

VOLUME XXVIII DECEMBER, 1955 NUMBER 6

The Pericardial Graft in Mitral Insufficiency

(A Morphological Study of the Aging Graft)

C. G. TEDESCHI, M.D. and HECTOR C. NAHAS, M.D., F.C.C.P

Philadelphia, Pennsylvania

Techniques applied to the surgical correction of mitral insufficiency have not yet reached the ideal stage of standardization as obtained in commissurotomy of mitral stenosis.

Murray, Wilkenson and McKenzie[1] (1938) attempted to correct mitral regurgitation experimentally produced in dogs by application of a graft which consisted of an inverted vein transplant, introduced through the left ventricle by means of a canula. The procedure aimed at the production of a flap or sling valve which would tamponate the mitral leak at each ventricular systole. The animals survived the operation and their postoperative life was significantly longer than those of the control group. Murray's experiments were repeated by Bailey and his associates[2] (1951) who noticed that the vein graft loses its resilience and becomes a shrunken fibrotic band.

Templeton and Gibbon[3] (1949) sutured pieces of pericardial tissue in dogs, as free grafts within the right auricle. These grafts were also found to become shrunken and fibrotic. Free grafts of pericardial tissue were then used intraventricularly in the same fashion as free vein graft. The graft functioned for a while but after a few weeks it became functionally inadequate, because of shrinking and fibrosis. In order to preserve the blood supply of the transplant, a pedicled, tubular pericardial graft was later applied by the Bailey group[4, 5] (1951). Since observations on dogs over a period of months indicated that these grafts functioned most adequately and showed no tendency to retract or become indurated, the method was subsequently applied to the human for the surgical correction of mitral insufficiency. In this so-called "ventricular pericardial tamponage" the pedicled graft is inserted through the wall of the left ventricle, made to pass between the chordea and the valve in proximity of the ostium and to function like a safety valve. Seven patients operated by this method showed some improvement, but subsequent attempts in 48 human beings were followed by high operative mortality (34.5 per cent) and the procedure was abandoned in favor of another. The new method, called "mitral suturing," consisted of suturing the incompetent portion of the valve leaflets with a free pericardial strip, tied in a lasso fashion. The long end of the pericardial strip was drawn out of the opening in the atrial or ven-

From the Division of Pathology and Department of Thoracic Surgery, Hahnemann Medical College and Hospital, Philadelphia 2, Pennsylvania.

tricular wall and securely fastened by an abbreviated purse-string suture. Twenty-two cases of mitral insufficiency treated by this method and followed for a six-month period were reported by Bailey in 1952.[6] The clinical results were satisfactory and the mortality reduced to 18 per cent. In the same report he mentioned three cases of "valvular suspension" achieved by running a pericardial strip across the free edge of the septal

SURGICAL CORRECTION OF MITRAL INSUFFICIENCY BY "GRAFT" METHOD

Author—Year	Experimental	Human	Material and Methods	Microscopic Observations on Graft
Murray, Wilkenson and McKenzie—1938	Dog		Transventricular approach. Vein graft	
Templeton and Gibbon—1949	Dog		Intra-auricular approach. Free pericardial graft	
C. P. Bailey and Assoc.—1951	Dog	x	Transventricular tamponade. Pedicled pericardial graft	
C. P. Bailey and Assoc.—1952		x	Trans-auricular or transventricular suturing. Free pericardial graft	
Glover and Assoc. —1952	Dog		Atrial or transventricular implant. Pedicled pericardial graft, tubular or opened	In atrial implant minimal change with maintenance of vascularity. In ventricular implant early swelling and later regressive change followed by scarring
C. P. Bailey and Assoc.—1952		x	Atrial or transventricular lasso. Valvular suspension. Free pericardial graft	
Moore and Shoemaker—1953	Dog		Transventricular approach, right or left ventricle. Free graft of vein, artery, tendon, pericardium, rectus fascia and peritoneum	Regressive change
Carter and Assoc.—1953	Dog		Transventricular approach. Prosthetic ball encased into pericardial pedicled tube	Regressive change
Harken and Assoc.—1954		x	Transauricular approach. Subvalvular prosthetic spindle baffle	

leaflet of the mitral valve and anchoring the free end at the apex of the ventricle. All three cases had good functional recovery and it was felt that the procedure had been instrumental in producing approximation of the valve during systole.

Moore and Shoemaker[7] (1953) made the first investigation in dogs of the fate of different types of transventricular autogenous slings. The study included two inverted arteries, four inverted veins, four tendons, two free pericardium, six pedicled pericardium, six rectus fascia and two peritoneum. The different slings, divided in equal numbers, had been introduced either through the left or the right ventricle. The arterial graft, placed in the right ventricle, showed after 49 days thrombus formation, was unelastic, fibrosed and contracted. The other arterial graft, placed in the left ventricle, examined after 79 days, was found to be ruptured and the stumps had retracted toward the mural endocardium giving rise to small swellings, which upon microscopic study revealed considerable intimal proliferation. The vein strings became all fibrotic and unelastic. These changes were more marked in the grafts placed in the left ven-

FIGURE 1: Pericardial sling six days after implantation showing marked swelling of the ventricular portion. Case 2, 24 year old white female submitted to double mitral commissurotomy and mitral suture.

tricle. There was intimal proliferation, media and adventitia displayed loss of normal structure, the elastic fibers were fragmented and there was widespread vacuolization. Tendon transplants presented thickening and hyalinization of collagen fibers with focal areas of cartilaginous metaplasia. The free pericardial graft, 11 days after operation, displayed swelling with thrombus formation near one end and upon microscopic examination the tissue was seen to have undergone extensive regressive change. Comparable lesions were found in a left pericardial sling eight days after implantation, also displaying organizing thrombus at one end and fibroblastic tissue proliferation at the other end, whereas the central area was acellular and amorphous.

Along the same line is a morphologic study of Glover and associates[8] (1953) of canine intracardiac pedicled, opened or tubular pericardial grafts at atrial or ventricular implantation. The animals were sacrificed at one week intervals from one to 15 weeks. Of three open grafts, two showed gross evidence of atrophy and fibrosis after five to 10 weeks but they were still very flexible; the third graft examined after four weeks revealed a large thrombus which occupied about one-third of the left auricle. None of the tubular grafts displayed evidence of thrombosis, thickening or inflexibility. After two to four weeks they remained incorporated within the atrial wall and upon histologic examination showed presence of numerous functioning blood vessels, a few of which contained organizing thrombi. Except for a few scattered areas of hyalinization the connective tissue was well preserved. The layers of rolled pericardium were fused by granulation tissue progressively rich in connective tissue

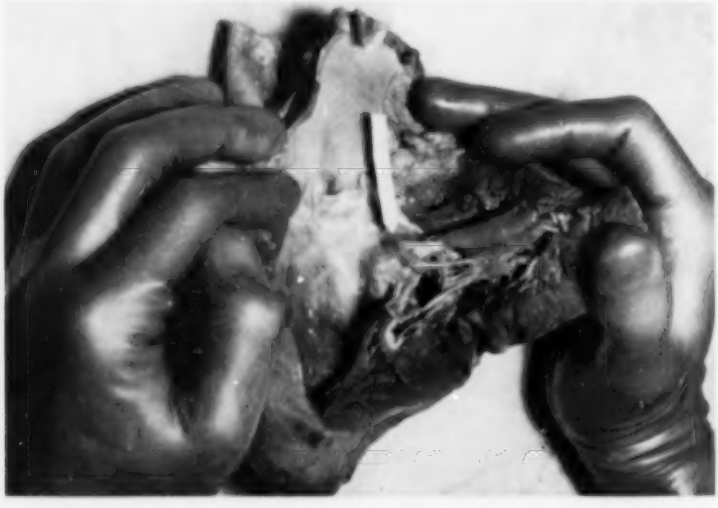

FIGURE 2: Adhesion of the pericardial sling by dense fibrous connective tissue to the septal leaflet of the mitral valve. Case 4, 22 year old white male, 45 days after mitral commissurotomy and suture.

fibers and the same process of fibroblastic tissue proliferation had resulted in fusion of the graft to the endocardium. No damage was noted in the adjacent myocardium. The transventricular grafts, in the first 48 hours, showed marked swelling with an increase in thickness up to twice as much as the original size so as to produce partial obstruction of the mitral orifice. At the end of the observation period, the portion of graft within the myocardial wall was found to be completely hyalinized and the portion lying free in the chamber of the ventricle was transformed into a thickened "myxomatous and unelastic strut." The myocardium surrounding the entrance and exit of the graft was widely replaced by fibrous tissue.

In view of the possibility that autogenous transplants may undergo regressive changes, Carter, Gould and Mann[9] (1953) have proposed the use of a prosthetic ball for the surgical correction of mitral insufficiency. In one group of dogs the plastic ball, encased in a transpericardial tube, was placed in between the mural leaflet and the mural endocardium via the transventricular approach; and in another group of dogs in a longer pericardial tube. Microscopic examination of the specimens obtained from the fifth day to two months after placement showed early avascular collagen transformation of the pericardial tube and they concluded that complete plastic prosthesis is preferable to the pericardial transplant.

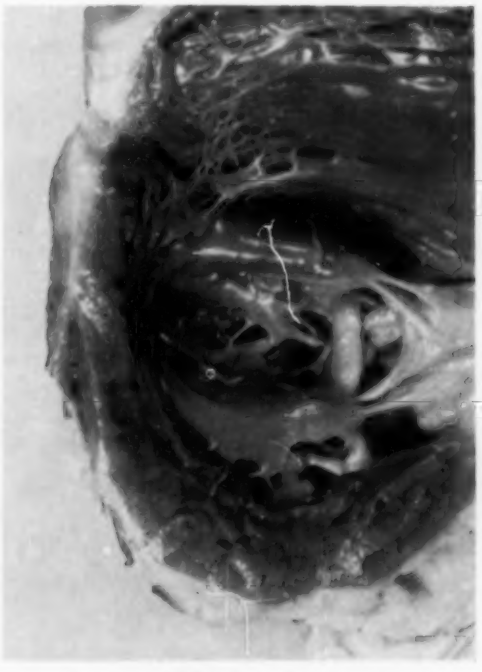

FIGURE 3: Intraventricular portion of pericardial sling, 22 months after implantation, adhering at many points to the chordae tendineae. Case 7, 43 year old white female submitted to transventricular pericardial tamponade and mitral commissurotomy.

Harken et al[10] (1954) have reported 16 cases of mitral insufficiency corrected by the application of a lucite, spindle-baggle type valve, placed transauricularly in the subvalvular region. There were three operative deaths and one later death. The fate of the survivals awaits further follow-up.

Personal Observations

Material and Method. In view of the uncertainties of the fate of the autogenous pericardial graft in the surgical correction of mitral insufficiency and of the criticisms which the method has received, mainly based on the presence of changes in the aging graft which are unfavorable from the functional standpoint, there is still need for morphologic observations.

The sequence of pathological changes in seven pericardial grafts in humans with mitral insufficiency is present in this report. In three cases the graft had been recently applied and the specimens were obtained three, six, and seven days after surgery. In the remaining four cases the graft was older, the specimens having been obtained 45 days, four months, 18 months and 22 months following surgery. In six instances the pericardial graft had been introduced through the auricle, made to pass through the valve leaflets and suspended to the auricular appendage. In the seventh case the graft had been placed by the transventricular method. The degree of tension of the lasso suture was evaluated by the operator's exploring

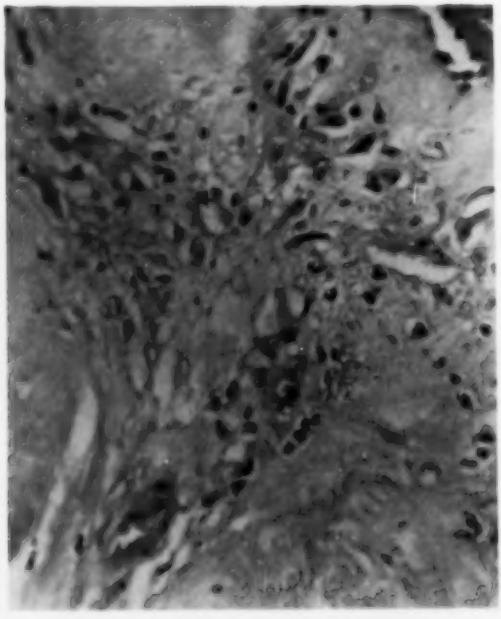

FIGURE 4: Microscopic appearance of pericardial sling 6 days after implantation showing swelling, edema and fibrinoid alteration of the ground substance. There is concurrent macrophagic activity and incipient fibroblastic cell proliferation. Case 2, Hematoxylin, Van Gieson stain, x80.

finger in perceiving the degrees of mitral regurgitation. Five cc. residual regurgitation was considered comparable with good operative result.

Case 1: A 55 year old white male with history of rheumatic disease at age of 10; he expired three days after surgery.

Autopsy (A54-20) revealed perforated pyloro-duodenal ulcer with gastric content spilled throughout the peritoneal cavity and formation of inflammatory exudate. The heart weighed 600 grams and showed enlargement of both ventricles. The thickness of the right ventricle wall was 10 mm. and that of the left 22 mm. The left and right auricles were dilated. The mitral suture lay along the valve opening lengthwise and attached its loop to the posterior commissure. The mitral valve anterolateral leaflet was thickened and slightly calcified and the posteromedial leaflet scarred and retracted. Anterior commissurotomy had been performed and the valve opening admitted the passage of two fingers. The aortic cusps showed a moderate degree of thickening with partial fusion of the left lateral commissure. Tricuspid and pulmonic valves were normal. The left anterior coronary artery showed patchy atherosclerosis without considerable narrowing of the lumen.

The pericardial sling had a dull appearance throughout and was thinly coated with fibrinous material. On the *microscopic sections* the fibrous connective tissue beneath the fibrinous exudate was edematous and infiltrated in scattered areas by granulation tissue containing prominent capillaries and fibroblasts. Toward the central portion, the sling displayed varying degrees of degeneration to actual necrosis in the absence of inflammatory changes.

Case 2: A 24 year old white female with history of rheumatic disease at the age of 14. She expired six days after double mitral commissurotomy and mitral suture.

Autopsy (A54-92) revealed extensive fibrinous pericarditis. The heart was markedly enlarged and weighed 840 grams. The wall of the right ventricle was 5 mm. in thickness and that of the left 14 mm. The left auricle was markedly dilated and presented patchy calcification of the mural endocardium. The mitral valve admitted the passage of two fingers and showed pronounced distortion and scarring of the leaflets.

The pericardial sling penetrated the mural leaflet nearby the posterior commissure and the anterior leaflet close to the anterior commissure. The auricular portion of the lasso was infiltrated with blood and its ventricular portion was markedly swollen to about six times the size of the auricular portion (Figure 1). *Microscopic sections* from

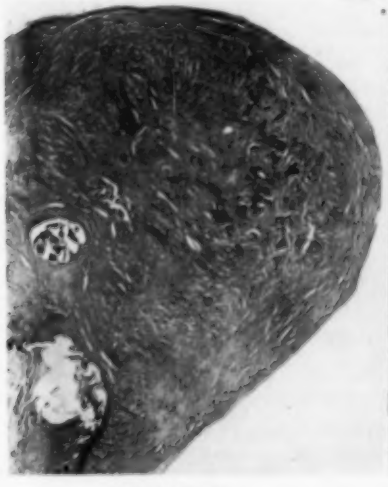

FIGURE 5

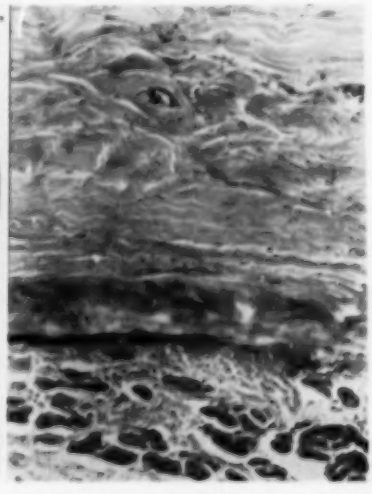

FIGURE 6

Figure 5: Microscopic appearance of the intraventricular portion of the graft, 22 months after implantation, displaying a few blood channels in the sclerosed and hyalinized pericardial sling. Case 7, Hematoxylin, van Gieson stain, x80.—*Figure 6:* Microscopic appearance of the intramyocardial portion of the graft of the same case Figure 5, showing bundles of poorly vascularized and almost completely hyalinized fibrous connective tissue. Hematoxylin, van Gieson stain, x80.

the ventricular portion of the sling showed its surface to be covered by deposits of fibrinous exudate. The subjacent fibrous connective tissue was edematous, and showed numerous arterioles with thickened, swollen walls and narrowed lumina. Small islands of fat were imbedded in the fibrous tissue. In the central portion of the sling the connective tissue was swollen, edematous and had undergone fibrinoid alteration of the ground substance (Figure 4). Lime-salt deposits were present here and there and it is likely that they pre-existed the surgical transplant of the pericardium. The middle third of the sling showed changes essentially similar to those seen in the ventricular portion. The superficial fibrinous exudate showed, however, incipient organization with replacement by granulation tissue rich both in blood channels and in mesenchymal cells. The portion of sling within the auricle revealed focal hemorrhage and granulocytic cell infiltration, beneath the peripheral fibrin deposits.

Case 3: A 30 year old white male with history of rheumatic disease at the age of 10. He expired seven days after mitral commissurotomy and mitral suture.

Autopsy findings (A54-68). The heart was enlarged and weighed 650 grams. The wall of the right ventricle was 6 mm. in thickness and that of the left 19 mm. The mitral valve was greatly distorted by calcium deposits and admitted the passage of one finger. The aortic cusps were thickened and partially fused at the lateral commissure.

The *pericardial sling* passed through the valve leaflets near the anterior commissure which showed recent thrombus formation. A 2 cm. long braided cotton thread was present on the ventricular aspect of the lasso which was less thick than the auricular portion. *Microscopic sections* both of the auricular and ventricular portions of the sling revealed in addition to recent thrombi, edema of the subjacent fibrous connective tissue with regressive change and focal fibroblastic tissue proliferation.

Case 4: A 22 year old white male with first attack of rheumatic disease at the age of six. Patient expired 45 days after mitral commissurotomy and suture.

Autopsy (A63-61) showed a large heart (480 grams) with considerable dilatation of the left ventricle. The right ventricle wall was 6 mm. thick and that of the left ventricle 16 mm. The mitral valve showed marked thickening and calcification, especially at the posterior commissure. The tendinous cords were thickened, shortened and fused together at many points. The tricuspid valve showed thickening of the leaflets and fusion of the commissure resulting in a funnel-like opening, 3 cm. in diameter.

The *pericardial sling* passed close to the anterior commissure, had a uniform fibrotic appearance and adhered by dense fibrous connective tissue (Figure 2) to the septal leaflet of the mitral valve which was distorted, sclerotic and calcified in places. *Microscopic examination* both of the auricular and ventricular portion of the sling showed diffuse scarring with foci of fibroblastic cell proliferation. Islands of adipose tissue were embedded in the superficial layers of the ventricular portion of the sling and they showed necrosis of fat cells with replacement by cellular fibrous connective tissue.

Case 5: A 30 year old Brazilian white female. This four months old sling was obtained through the courtesy of Dr. Bailey. The patient had been operated on in a hospital in Brazil for mitral insufficiency. *Microscopic sections* revealed a hyalinized cord of fibrous tissue, with occasional foreign body type giant cells, blood capillaries and fibroblasts near the periphery. Small foci of calcification, edema and degeneration were present in the central portion.

Case 6: (A54-21). A 24 year old white male with history of rheumatic disease at the age of nine. In July, 1952, he was operated of mitral suture and discharged in good condition. In January, 1954, he was operated again and this time the operation consisted of insertion of Hufnagel valve. At the end of the procedure the patient developed ventricular fibrillation and irreversible cardiac arrest.

Autopsy (A54-21). The heart weighed 660 grams and showed hypertrophy of the wall of the right and left ventricles, 9 and 25 mm. in thickness respectively. The mitral valve opening admitted three fingers and the aortic valve opening two fingers. Both showed evidence of healed valvulitis with thickening and retraction of the leaflets and cuspid edges.

The *pericardial sling* was fibrosed throughout, adhered to the mitral valve leaflets and was firmly attached to the auricular wall. The *microscopic sections* revealed an almost completely acellular, poorly vascularized, hyalinized cord of fibrous tissue which in small areas was edematous and granular. There were sparse collections of lymphocytes.

Case 7: This 43 year old white female had rheumatic fever at the age of 12 with onset of heart failure at the age of 38. She was operated on for mitral insufficiency on January 22, 1952 by a transventricular pericardial tamponade. On October 16, 1953 and on September 27, 1954, mitral commissurotomy was performed. She died December 21, 1954.

At post mortem the heart weighed 530 grams. The walls of both ventricles were

hypertrophied (left 16 mm. and right 9 mm.). The mitral valve opening admitted two fingers and presented fibrous thickening of both leaflets with shortening of the chorda tendineae and hypertrophy of the papillary muscles. The anterior commissure showed evidence of commissurotomy 0.5 cm. in depth. The remaining valves were not remarkable.

The *pericardial sling* penetrated into the left ventricle about 1.5 cm. from the interventricular septum below the posterior commissure of the mitral valve, extended anterolaterally and was inserted into the left ventricle wall 4 cm. from the interventricular septum. In its course it fused to several adjacent chordae tendineae (Figure 3). The intraventricular portion of the graft was firm, smooth and whitish-gray and measured 3 cm. in length with a width ranging from 7 to 4 mm. in diameter.

Microscopic sections of the intraventricular portion of the graft showed it to be almost completely hyalinized and avascular (Figure 5). Its surface was smooth and no cellular lining could be made out. The epicardial end of the graft as well as the intramyocardial portions were hyalinized also (Figure 6) and contained occasional small, narrow vascular channels. The surrounding myocardium presented zones of fibrosis which delineated the graft rather sharply from the heart muscle.

Comment

Survey of the changes encountered in seven aging pericardial strips, from three days to 22 months after implantation according to surgical procedure — mitral commissurorrhapy — devised for the correction of mitral insufficiency,[11] brings up several points which deserve comment.

Swelling of the strip was a consistent finding in the specimens obtained at the third, fifth and seventh day following surgery. In two specimens (six and seven days old) the swelling had resulted in an increase of thickness of the strip from two to six times the original size. Obstruction of the mitral valve opening is a forseeable complication resulting from the swelling of the pericardial transplant.

In two of our older specimens (case 4 and 5), the pericardial strip was found to adhere to the midpoint of the valve leaflets by dense fibrous connective tissue. From the dynamic standpoint, this pericardial valvular symphysis must be regarded as an unfavorable result, inasmuch as it can produce fixation of the valve either in regurgitation or in stenotic position. This complication might be avoided by placing the pericardial suture at the commissure.

A recent thrombus was noticed on the pericardial transplant of case 2 and its fragmentation was found to have caused embolic phenomena resulting in multiple renal infarcts. In all our cases the nature of the involutional changes that the pericardial strips were undergoing predisposed to local thrombus formation although evidence of this complication was found in one case only. Since in this specific case there was concurrent calcification of the valve, freshly cut by commissurotomy and a foreign body represented by braided cotton, one is inclined to ascribe the thrombosis to these particular conditions.

Our observations indicate that the transplanted pericardium undergoes early regressive changes and that the degenerated areas are promptly replaced by a granulation tissue. This becomes progressively richer in fibroblastic tissue and poorer in blood vessels. The resulting structure is a firm band of sclerosed fibrous connective tissue. In view of the paucity of blood vessels, it must be assumed that nutrition is drawn from the intracardiac blood.

SUMMARY

Techniques applied to surgical correction of mitral insufficiency include the application of autogenous pericardial grafts. The sequence of pathological changes in seven pericardial grafts in humans with mitral insufficiency is here presented. The age of the grafts ranged from three days to 22 months. Regressive changes were noticed in the early transplants and they were followed by subsequent proliferation of granulation tissue. Ultimately the graft was seen to consist of a sclerosed, poorly vascularized band of fibrous connective tissue. Swelling of the strip was constantly found in specimens obtained at the third, fifth, and seventh day following surgery. Secondary obstruction of the mitral valve opening is a possible complication related to this alteration. In two of the older specimens obtained 45 days and six months after surgery, the pericardial strip was seen to adhere to the valve leaflets by dense fibrous connective tissue. This also must be regarded as an unfavorable result inasmuch as it can produce fixation of the valve either in regurgitation or in stenotic position.

RESUMEN

Las técnicas empleadas para la corrección de la insuficiencia mitral incluyen la aplicación de injertos autógenos pericardiacos. Se presenta la evolución de los cambios patológicos en siete injertos pricárdicos en seres humanos con insuficiencia mitral. La edad de los injertos era de tres días a 22 meses. Se notaron cambios regresivos en los transplantes primeros y estos eran seguidos por proliferación de tejido de granulación. Al fin el injerto se vió que consistía en una banda de tejido conectivo fibroso, esclerosso y pobremente vascularizada.

Hinchazón de la banda se encontró constantemente en especímenes obtenidos al tercero, quinto, sexto días después de la cirugía. Una posible complicación es la obstrucción secundaria de la abertura de la válvula mitral en relación con esta laceración. En dos de los especímenes más antiguos obtenidos 45 días y seis meses después de la operación se vió que la banda pericárdica se adhería a las hojillas de la válvula por tejido conectivo denso. Esto debe verse también como un resultado desfavorable puesto que puede producir fijación de la válvula ya sea en regurgitación o en posición estenótica.

RESUME

Les procédés techniques utilisés pour l'amélioration de l'insuffisance mitrale par la chirurgie comprennent l'application de greffes péricardiques autogènes. Les auteurs présentent la série des modifications pathologiques survenues chez sept individus atteints d'insuffisance mitrale et porteurs de greffes péricardiques. L'âge des greffes va de trois jours à 22 mois. Des altérations régressives furent notées dans les greffes précoces, et elles furent suivies de prolifération de tissu de granulation. En dernier lieu, la greffe finit par devenir une zone de tissu fibreux conjonctif sclérosé, et faiblement vascularisé. L'oedème de la bande fut constamment trouvée au 3ème, 5ème et 7ème jours suivant l'intervention. L'obstruction secon-

daire de la valvule mitrale gênant son ouverture est une complication possible de cette altération.

Dans deux des cas les plus anciens, après 45 jours à 6 mois à dater de l'intervention, la bande péricardique sembla adhérer aux clapets de la valvule par du tissu conjonctif fibreux dense. Cice peut être considéré comme un résultat défavorable en tant qu'il peut n'apporter aucune amélioration, soit à cause de la régurgitation, soit à cause de la formation de sténose.

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Tuberculosis Among Nurses*

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The Problem

For centuries tuberculosis exacted a large toll in health and life among those who took care of tuberculous persons. Isocrates (436-338 B.C.) called attention to such observations of his time. The disease among those who cared for tuberculous patients apparently continued unabated through the ages. Despite recognition of the problem as manifested by references from time to time, no effective solution was devised until the present century.

In 1920 and for a few succeeding years, our observations consisted largely of diagnosing tuberculosis among student and graduate nurses after symptoms had appeared when the disease was advanced and contagious. Although in the areas where the majority of these students were reared tuberculosis mortality, morbidity and infection attack rates were decreasing, there was definite increase among student nurses.

It was well known that tuberculosis is caused by the tubercle bacillus, that practically everyone is born free from this organism, and that infections are acquired from direct or indirect contact with persons or animals eliminating tubercle bacilli. With so much information available, an attempt to solve the problem among nurses seemed logical. Moreover, if the nursing profession could not solve its own problem, the public would not be expected to manifest confidence in its ability to effectively participate in the general tuberculosis eradication movement. As long as the disease in students was diagnosed after it had reached an advanced

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We are especially indebted to Mrs. Eleanor Sundstrom, Mrs. Kaye Swedien and Mr. Paul Rupprecht for their invaluable participation in assembling, tabulating, and analyzing data.
Much credit is due administrators, nursing and medical staffs, and personnel of x-ray departments of these hospitals for their excellent co-operation.
The students and graduates of these schools of nursing, through their fine co-operation while students and their excellent response since graduation, contributed greatly to the success of this study.

stage, the problem continued undiminished. Obviously, the attack must be made on the tubercle bacillus itself rather than just the gross disease it has produced.

Program Launched

In 1927 a long-term study was launched in an attempt to learn how to control tuberculosis among nurses. It was known that within a few weeks after tubercle bacilli invade the human body, the tissues, including the skin, become sensitized to tuberculo-protein. Therefore, by the tuberculin test one could identify persons harboring tubercle bacilli. Postmortem experience had revealed that those who react characteristically to tuberculin have tuberculous lesions in various parts of their bodies. Evidence was later adduced to show that reactors are harboring tubercle bacilli. Thus the tuberculin reaction indicates the presence of tubercle bacilli in the individual's body. With such a specific and accurate test available, all students in whom tubercle bacilli resided could be identified.

Several schools of nursing were selected. In one designated School II in previous reports, there was such lack of cooperation that it was later omitted. There remained Fairview, Swedish, St. Mary's and University Schools of Nursing. The Minneapolis General Hospital organized a new school in 1947 which was added to our group.

At first (1927) in each of these schools the tuberculin testing program was offered the senior classes. However, the majority of the other students requested it. In 1928, nearly all students were tested and in 1929 each class became a part of our regular program. All entering students were given 0.1 milligram of tuberculin intracutaneously. Those who presented no reaction within 48 to 72 hours received 1.0 milligram. Thus students were divided into two groups: 1. Those who had been infected and were harboring tubercle bacilli on admission; 2. Those who had not been infected. Students who did not react to tuberculin on admission had the test administered semiannually as long as they were nonreactors.

Although these schools had no responsibility for infections which had occurred prior to entrance, they were accountable for most of those acquired by students while in school.

Students who reacted on admission were promptly examined, including x-ray film inspection of the chest. On a number of occasions they themselves presented previously unsuspected clinical lesions on entrance. If no clinical disease was found, they had such examinations semiannually. Each student who became a reactor while in school was placed on the list for periodic examinations.

From 1943 to 1949 inclusive, Dr. Carroll E. Palmer, Director, Field Studies, Division of Tuberculosis, United States Public Health Service, conducted a nationwide study on tuberculosis among students of nursing. Our schools participated in this program and his teams did the tuberculin testing, using purified protein derivative (PPD) and x-ray work during those years. However, he kindly made his findings available to use throughout this period so there was no break in the continuity of our study.

The tuberculin test proved to be the master key. It not only determined the presence of tuberculosis earlier than any other phase of an examination but also detected offending situations promptly. For students who entered uninfected, periodic testing with tuberculin afforded the earliest possible diagnosis in those who became infected. Moreover, when an individual converted, we knew there had been contact with a contagious case of tuberculosis since the last negative test. In point of time the contact was near and it was usually possible to track down the source of the student's infection to an affiliated hospital or sanatorium, to a department within the home school, and not infrequently to the room or ward of a previously unsuspected case.

Such information was of extreme value for it was excellent reason to discontinue certain services and to correct others. For example, the problem of persons entering hospitals with authentic nontuberculous conditions but having co-existing contagious tuberculosis which was not detected on admission was brought to light in many cases by student nurses converting to tuberculin reactors, after which the source was found in such a patient. This had occurred so often that it was recognized as a serious but controllable problem.

In 1933 the management and medical staff of Swedish Hospital conducted a two-month demonstration which consisted of tuberculin testing all patients on admission as well as personnel members. Reactors had examinations completed. The number of unsuspected cases of tuberculosis found was such as to recommend the procedure as routine. However, largely because of cost of x-ray films, it was not continued.

In 1935, one of us (H. S. D.) became Dean of Medical Sciences, University of Minnesota, and arranged for admission examinations for tuberculosis of all patients. This consisted of the tuberculin test, x-ray film inspection of the chests of reactors, and completing the examination of all who had shadow-casting lesions that might be tuberculous. Because of a few days delay in administering and reading tuberculin tests, this was later changed to an admission chest x-ray film of each patient and the tuberculin test was done later. The first year this procedure was in effect, 48 persons were found entering the hospital for nontuberculous conditions who had co-existing tuberculosis. The patient admission examination was so effective and revealing from year to year that it has since been routine.

There was also the problem of tuberculosis among both professional and nonprofessional hospital personnel. The first year hospital admissions were examined, University Hospital personnel members were surveyed. Three were found to have contagious tuberculosis concerning which the institution had no previous knowledge. Each was in contact with our student nurses. Nature and extent of disease, together with duration of employment, left little doubt but that each of them had contagious disease when they were employed, but they were not examined at that time. This emphasized the importance of pre-employment examinations, which have been routine since 1936. Moreover, every employee is re-ex-

amined semiannually. In 1938 this program for both admissions and employees was adopted at the Minneapolis General Hospital where students of the University School of Nursing devoted considerable time. This was an excellent demonstration for the other hospitals included in our group. However, they were slow to adopt it. Indeed, it had often been said that because of difficulty of convincing hospital medical and nursing staffs, as well as administrators, the adoption of this program in some institutions would occur only through enactment of law, requirements of insurance companies, attorneys, civil courts, and industrial commissions.

In 1947, a law was enacted which provided that any student nurse, medical student, or medical intern who contracted tuberculosis as a result of direct contact with tuberculous patients during the course of training in a tax-supported institution would be provided treatment by the state or county in which the infection occurred. This later came to apply to other hospitals and institutions training nurses. This was a boon in our effort to protect student nurses against tuberculosis, as legal action was brought against several hospitals which, almost without exception, was decided in favor of students.

The program was encouraged by a great many persons who had read our early reports concerning the seriousness of the problem. From another state came this statement from a physician in 1934, "I note with interest that your tuberculosis hospitals have suddenly changed status from institutions where tuberculosis is supposed to be cured to pest incubators where it is generated and spread! Your frankness however is to be tremendously congratulated." A physician from another state wrote in 1934, "I am sure it is the beginning of an awakening by the schools of nursing as to their responsibility." In December, 1937, a teacher from another city wrote the president of the University of Minnesota, making many inquiries such as, "The campaign against tuberculosis attempts to save lives. Why overlook the nurse?" "Is there not need for action?"

While seeking methods to solve the tuberculosis problem among students of nursing, the literature was thoroughly investigated. A large number of so-called immunizing agents had previously been recommended. However, it had been proved conclusively in the 1880's that tuberculosis differs from such diseases as smallpox, typhoid fever, and diphtheria in that neither a mild nor severe attack leaves the individual with dependable immunity. Tuberculosis is notoriously a relapsing disease. Therefore, the futility of attempting to produce immunity artificially was recognized.

Of all methods considered the only one that seemed sound was to manage tuberculosis as a contagious disease. This again meant attacking the tubercle bacillus rather than just the gross damage it had done.

Contagious Disease Technique

When this study began, effective contagious disease technique was employed for such bacterial diseases as diphtheria and typhoid fever. Why this had not been adopted in tuberculosis was an enigma. There was no

reason to believe it would not be efficacious. After much persuasion, one hospital with a tuberculosis service instituted medical asepsis. This slightly reduced the incidence of infection acquired by students, but its inadequacy was obvious.

In the early 1930's, the first attempt was made to institute rigid contagious disease technique on a small tuberculosis service in the University Hospital. From this small beginning, the technique was gradually perfected. In 1940 it was introduced on a chest disease service in the Minneap-

TABLE I
FAIRVIEW SCHOOL OF NURSING

		REACTORS				NONREACTORS				CONVERTERS DURING TRAINING	
		Entrance		Graduation		Entrance		Graduation			
Year	No. in Class	No.	Per cent	No.	Per cent	No.	Per cent	No.	Per cent	No.	Per cent
*1930	27	2	7.4	27	100.0	25	92.6	0	0.0	25	100.0
1931	27	1	3.7	22	81.5	26	96.3	5	18.5	21	80.8
1932	28	6	21.4	27	96.4	22	78.6	1	3.6	21	95.5
1933	35	4	11.4	32	91.4	31	88.6	3	8.6	28	90.3
1934	19	4	21.1	19	100.0	15	79.0	0	0.0	15	100.0
1935	28	6	21.4	25	89.3	22	78.6	3	10.7	19	86.4
1936	22	2	9.1	17	77.3	20	90.9	5	22.7	15	75.0
1937	22	3	13.6	17	77.3	19	86.4	5	22.7	14	73.7
1938	38	2	5.3	16	42.1	36	94.7	22	57.9	14	38.9
1939	26	8	30.8	14	53.9	18	69.2	12	46.2	6	33.3
1940	31	8	25.8	18	58.1	23	74.2	13	41.9	10	43.5
1941	33	2	6.1	7	21.2	31	93.9	26	78.8	5	16.1
1942	39	1	2.6	7	18.0	38	97.4	32	82.1	6	15.8
1943	25	3	12.0	4	16.0	22	88.0	21	84.0	1	4.6
1944	42	4	9.5	7	16.7	38	90.5	35	83.3	3	7.9
1945	51	7	13.7	7	13.7	44	86.3	44	86.3	0	0.0
1946	52	7	13.5	15	28.9	45	86.5	37	71.2	8	17.8
1947	77	4	5.2	8	10.4	73	94.8	69	89.6	4	5.5
1948	68	7	10.3	10	14.7	61	89.7	58	85.3	3	4.9
1949	47	0	0.0	8	17.0	47	100.0	39	83.0	8	17.0
1950	48	4	8.3	5	10.4	44	91.7	43	89.6	1	2.3
1951	64	4	6.3	12	18.8	60	93.8	52	81.3	8	13.3
1952	53	2	3.8	8	15.1	51	96.2	45	84.9	6	11.8
1953	64	2	3.1	4	6.3	62	96.9	60	93.8	2	3.2
1954	67	4	6.0	8	11.9	63	94.0	59	88.1	4	6.4
TOTAL	1033	97		344		936		689		247	

*Records were incomplete and contact could not be made with 2 in the Class of 1930. They are not included in this report.

olis General Hospital where it has since been in continuous operation. Its value in protecting students has been thoroughly demonstrated. It has been said that a tuberculosis service is the safest place for students, but our observations revealed the erroneousness of this belief, unless rigid contagious disease technique is employed.

Results

For many years the Fairview Hospital had a separate building which housed about 70 patients with advanced tuberculosis. All students were compelled to spend three months on this service without benefit of contagious disease technique. About 1930 the separate building was abandoned and the patients were moved to a wing of the main building. Medical asepsis was introduced and the percentage of tuberculin conversions dropped only to 80.7 in the class of 1931 (Table I, figure 1) but in the class of 1934, it was back to 100.

When the tuberculosis service was discontinued in 1935 and subsequent patients were treated under contagious technique in single rooms, the percentage of converters remained above 70 for the next two years. Although students in these two classes did not work on a tuberculosis service as such, they were in the hospital while the service was still in

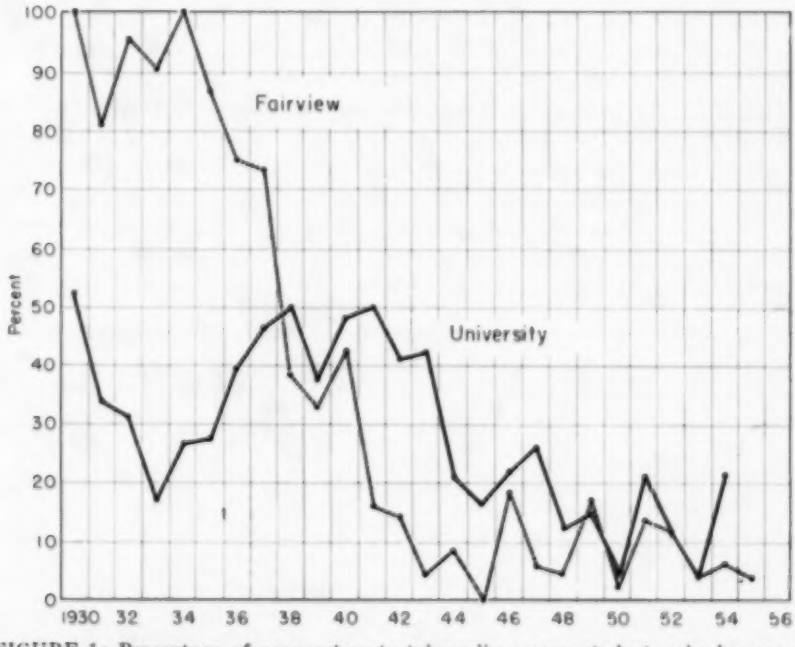

FIGURE 1: Percentage of nonreactors to tuberculin among students who became reactors during training in Fairview and University Hospital schools of nursing. Peaks in the graphs since 1938 indicate inadequate diagnoses, temporary employment of unapproved procedures, and breaks in contagious disease technique.

operation. Unless contagious disease technique is rigidly enforced, we do not believe it is possible to have a tuberculosis service in a hospital without tubercle bacilli being disseminated throughout the building. The class of 1938 was the first to enter the school after the tuberculosis service was discontinued and the incidence of tuberculin converters in this class on graduation was less than 40 per cent.

The increase in percentage of reactors on graduation in the classes of 1939 and 1940 (figure 1) was due to a comatose diabetic patient who was in the institution for almost two weeks and tuberculosis was not detected until necropsy. Only the tuberculin test determined which students acquired primary tuberculosis (tuberculous infection) as the x-ray films of their chests at that time were clear. Following this episode, there was a precipitous decrease in the infection attack rate and the goal was reached in the class of 1945, when no student who entered in 1942 as a nonreactor to tuberculin had become infected through the senior year. About that time and without our knowledge, the director of the school arranged an affiliation with a tuberculosis service in another hospital where only medical asepsis was employed. A few students became infected with resulting litigation. An affiliation was then established with another hospital in July, 1951, where the chest disease service is operated under strict contagious disease technique (figure 1). Thus, since 1945, a few students have been infected, but all except one occurred outside this hospital. This one was exposed to an elderly patient whose pulmonary lesions had been diagnosed as nontuberculous until tubercle bacilli were found in his sputum while in the hospital.

The Minneapolis General Hospital School was organized in 1947. This institution has a chest disease service operated under contagious disease technique where all students receive training in tuberculosis (Table II).

St. Mary's Hospital admitted the occasional tuberculous patient in the earlier years of this study and in 1937 established a chest surgery service to which a considerable number of contagious tuberculous cases have since been admitted. Students had a few weeks training on a general contagious

TABLE II
MINNEAPOLIS GENERAL HOSPITAL SCHOOL OF NURSING

		REACTORS				NONREACTORS				CONVERTERS DURING TRAINING	
		Entrance		Graduation		Entrance		Graduation			
Year	No. in Class	No.	Per cent	No.	Per cent	No.	Per cent	No.	Per cent	No.	Per cent
1950	17	1	5.9	2	11.8	16	94.1	15	88.2	1	6.3
1951	38	5	13.2	9	23.7	33	86.8	29	76.3	4	12.1
1952	22	1	4.6	1	4.6	21	95.4	21	95.4	0	0.0
1953	31	3	9.7	6	19.4	28	90.3	25	80.6	3	10.7
1954	32	6	18.7	12	37.5	26	81.3	20	62.5	6	23.1
1955	32	3	9.4	7	21.9	29	90.6	25	86.2	4	12.5
TOTAL	172	19		37		153		135		18	

disease service in another hospital before being assigned to the chest disease service. The sharp rises in percentage of converters in the classes of 1940 and 1946 were due to unusual incidences. In 1943, although this school had a chest disease service, an affiliation was established with a sanatorium which insisted upon students being infected with tubercle bacilli before taking the service and therefore administered BCG to those who consented. This affiliation was discontinued in 1949. Following the low incidence in the class of 1946, there was a continuous rise for several years suggesting that contagious disease technique was not rigidly practiced or that unsuspected cases were admitted to other parts of the hospital. The situation markedly improved in the classes of 1954 and 1955 (Table III, figure 2).

Swedish Hospital has not had a tuberculosis service as such or has it had an affiliation with another institution for teaching students tuberculosis. However, unsuspected cases of tuberculosis have been admitted and, more recently, the occasional known case. Although this hospital demonstrated the importance of examining all patient admissions and personnel members in 1933, the project was abandoned at the end of the demonstration. The incidence of converters increased and reached the height of 45.5 per cent in the class of 1938. This stimulated institution of better protective measures which have been reasonably satisfactory except in the classes of

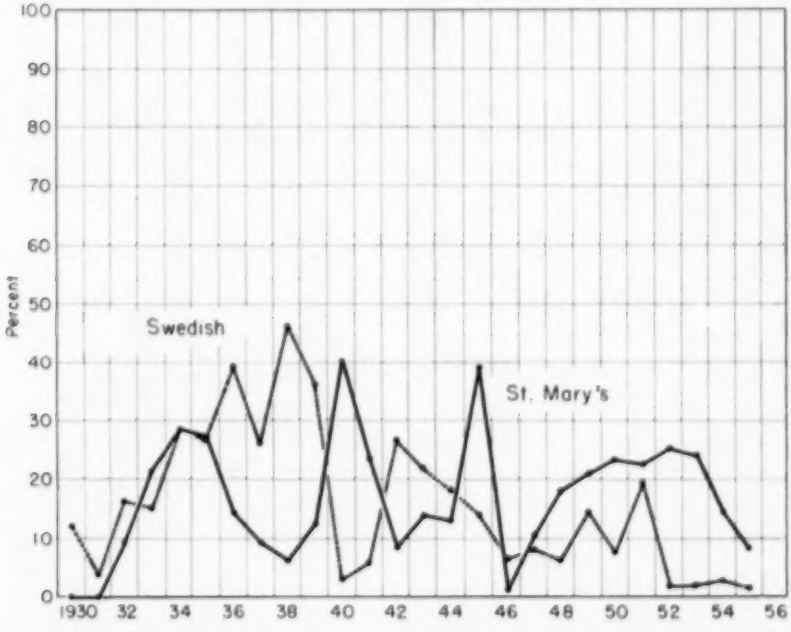

FIGURE 2: Percentage of nonreactors to tuberculin among students who became reactors during training in St. Mary's and Swedish Hospital schools of nursing. Peaks in the graphs since 1938 indicate inadequate diagnoses, temporary employment of unapproved procedures, or breaks in contagious disease technique.

1942 and 1951, caused by oversights in diagnosis and technique. During the past four years, the percentage of converters has been approximately 2 (Table IV, figure 2).

In the University School, students have been well protected since 1936 by examination of patient admissions and personnel members. However, this school has long had a sanatorium affiliation where, in earlier years, students spent six weeks in residence working with contagious cases. Since November, 1940, reactors have worked with contagious patients

TABLE III
ST. MARY'S SCHOOL OF NURSING

		REACTORS				NONREACTORS				CONVERTERS DURING TRAINING	
		Entrance		Graduation		Entrance		Graduation			
Year	No. in Class	No.	Per cent	No.	Per cent	No.	Per cent	No.	Per cent	No.	Per cent
*1930	32	20	62.5	20	62.5	12	37.5	12	37.5	0	0.0
*1931	35	25	71.4	25	71.4	10	28.6	10	28.6	0	0.0
1932	37	6	16.2	9	24.3	31	83.8	28	75.7	3	9.7
1933	38	10	26.3	16	42.1	28	73.7	22	57.9	6	21.4
1934	32	7	21.9	14	43.8	25	78.1	18	56.3	7	28.0
*1935	44	3	6.8	14	31.8	41	93.2	30	68.2	11	26.8
1936	39	4	10.3	9	23.1	35	89.7	30	76.9	5	14.3
*1937	27	6	22.2	8	29.6	21	77.8	19	70.4	2	9.5
*1938	22	5	22.7	6	27.3	17	77.3	16	72.7	1	5.9
1939	49	9	18.4	14	28.6	40	81.6	35	71.4	5	12.5
1940	38	8	21.1	20	52.6	30	79.0	18	47.4	12	40.0
1941	51	5	9.8	16	31.4	46	90.2	35	68.6	11	23.9
1942	32	9	28.1	11	34.4	23	71.9	21	65.6	2	8.7
1943	42	5	11.9	10	23.8	37	88.1	32	76.2	5	13.5
1944	46	8	17.4	13	28.3	38	82.6	33	71.7	5	13.2
1945	65	7	10.8	30	46.2	58	89.2	35	53.9	23	39.7
1946	79	9	11.4	10	12.7	70	88.6	69	87.3	1	1.4
1947	102	5	4.9	15	14.7	97	95.1	87	85.3	10	10.3
1948	54	3	5.6	12	22.2	51	94.4	42	77.8	9	17.7
1949	49	1	2.0	11	22.5	48	98.0	38	77.6	10	20.8
1950	42	3	7.1	12	28.6	39	92.9	30	71.4	9	23.1
1951	45	0	0.0	10	22.2	45	100.0	35	77.8	10	22.2
1952	62	6	9.7	20	32.3	56	90.3	42	67.7	14	25.0
1953	51	6	11.8	17	33.3	45	88.2	34	66.7	11	24.4
1954	43	2	4.7	8	18.6	41	95.4	35	81.4	6	14.6
TOTAL	1156	172		350		984		806		178	

*Records were incomplete and contact could not be made with 1 in 1930, 1 in 1931, 1 in 1935, 1 in 1937 and 1 in 1938. They are not included in this report.

while uninfected students have spent two weeks there in contact only with noncontagious cases. This apparently resulted in a precipitous decrease in tuberculin converters. However, unusually high peaks occurred in the classes of 1947, and 1954. Since 1937, the percentage of converters in this school has remained higher than the Fairview School except the class of 1949 (Table I and V, figure 1).

We have had no direct control over the methods employed in these schools of nursing. Our function has been to make semiannual examina-

TABLE IV
SWEDISH SCHOOL OF NURSING

		REACTORS				NONREACTORS				CONVERTERS DURING TRAINING	
		Entrance		Graduation		Entrance		Graduation			
Year	No. in Class	No.	Per cent	No.	Per cent	No.	Per cent	No.	Per cent	No.	Per cent
*1930	19	2	10.5	4	21.1	17	89.5	15	79.0	2	11.8
*1931	36	0	0.0	1	2.8	36	100.0	35	97.2	1	2.8
*1932	56	6	10.7	14	25.0	50	89.3	42	75.0	8	16.0
1933	43	10	23.3	15	34.9	33	76.7	28	65.1	5	15.2
1934	30	5	16.7	12	40.0	25	83.3	18	60.0	7	28.0
1935	34	4	11.8	12	35.3	30	88.2	22	64.7	8	26.7
1936	27	4	14.8	13	48.2	23	85.2	14	51.9	9	39.1
1937	34	7	20.6	14	41.2	27	79.4	20	58.8	7	25.9
1938	44	11	25.0	26	59.1	33	75.0	18	40.9	15	45.5
1939	45	17	37.8	27	60.0	28	62.2	18	40.0	10	35.7
1940	39	8	20.5	9	23.1	31	79.5	30	76.9	1	3.2
*1941	48	9	18.8	11	22.9	39	81.3	37	77.1	2	5.1
*1942	39	2	5.1	12	30.8	37	94.9	27	69.2	10	27.0
1943	47	10	21.3	18	38.3	37	78.7	29	61.7	8	21.6
1944	48	9	18.8	16	33.3	39	81.3	32	66.7	7	18.0
1945	63	10	15.9	17	27.0	53	84.1	46	73.0	7	13.2
1946	66	10	15.2	14	21.2	56	84.9	52	78.8	4	7.1
1947	56	4	7.1	8	14.3	52	92.9	48	85.7	4	7.7
1948	51	6	11.8	9	17.7	45	88.2	42	82.4	3	6.7
1949	38	2	5.3	7	18.4	36	94.7	31	81.6	5	13.9
1950	66	14	21.2	18	27.3	52	78.8	48	72.7	4	7.7
1951	49	7	14.3	15	30.6	42	85.7	34	69.4	8	19.1
1952	56	6	10.7	7	12.5	50	89.3	49	87.5	1	2.0
1953	52	4	7.7	5	9.6	48	92.3	47	90.4	1	2.1
1954	81	5	6.2	7	8.6	76	93.8	74	91.4	2	2.6
TOTAL	1167	172		311		995		856		139	

*Records were incomplete and contact could not be made with 12 in 1930, 8 in 1931, 1 in 1932, 2 in 1941 and 4 in 1942. They are not included in this report.

tions of students, using tuberculin, x-ray film inspection, etc. as indicated. For the most part, our recommendations have been accepted. However, on occasion, unapproved procedures were practiced which resulted in at least temporary increase of tuberculin conversions. These interruptions usually resulted from changes of directorships. Some new directors were not familiar with our program and at first caused considerable interruption. However, in most instances, these schools have been most cooperative. Peaks in the graphs, particularly since 1938, have been due to temporary adoption of unapproved procedures, errors in diagnosis, or breaks in contagious technique.

TABLE V
UNIVERSITY SCHOOL OF NURSING

		REACTORS				NONREACTORS				CONVERTERS DURING TRAINING	
		Entrance		Graduation		Entrance		Graduation			
Year	No. in Class	No.	Per cent	No.	Per cent	No.	Per cent	No.	Per cent	No.	Per cent
1930	58	25	43.1	36	62.1	33	56.9	22	37.9	11	33.3
1931	74	29	39.2	43	58.1	45	60.8	31	41.9	14	31.1
1932	75	21	28.0	42	56.0	54	72.0	33	44.0	21	38.9
1933	30	10	33.3	16	53.3	20	66.7	14	44.7	6	30.0
1934	21	6	28.6	17	81.0	15	71.4	4	19.0	11	73.3
1935	44	9	20.5	19	43.2	35	79.5	25	56.8	10	28.6
1936	75	9	12.0	36	48.0	66	88.0	39	52.0	27	40.9
1937	52	8	15.4	31	59.6	44	84.6	21	40.4	23	52.3
1938	88	23	26.1	52	59.1	65	73.9	36	40.9	29	44.6
1939	82	18	22.0	50	61.0	64	78.0	32	39.0	32	50.0
1940	21	2	9.5	11	52.4	19	90.5	10	47.6	9	47.4
1941	8	2	25.0	5	62.5	6	75.0	3	37.5	3	50.0
1942	86	27	31.4	57	66.3	59	68.4	29	33.7	30	50.8
1943	60	15	25.0	31	51.7	45	75.0	29	48.8	16	35.6
1944	93	15	16.1	30	32.3	78	83.9	63	67.7	15	19.2
1945	129	23	17.8	50	38.8	106	82.2	79	61.2	27	25.5
1946	253	49	19.4	96	37.9	204	80.6	157	62.1	47	23.0
1947	199	21	10.6	70	35.2	178	89.4	129	64.8	49	26.8
1948	184	29	15.8	60	32.6	155	84.2	124	67.4	31	20.0
1949	72	9	12.5	20	27.8	63	87.5	52	72.2	11	17.5
1950	38	3	7.9	7	18.4	35	92.1	31	81.6	4	12.1
1951	30	1	3.3	8	26.7	29	96.7	22	73.3	7	25.0
1952	55	4	7.3	10	18.2	51	92.7	45	81.8	6	11.8
1953	45	3	6.7	5	11.1	42	93.3	40	88.9	2	4.8
1954	76	5	6.6	20	26.3	71	93.4	56	73.7	15	21.1
TOTAL	1948	366		822		1582		1126		456	

In none of these schools has the conversion problem been completely solved. However, the situation has been markedly improved. Prior to 1927, tuberculosis was in a chaotic state. Students were afforded no protection against tubercle bacilli from patients in sanatoriums, general hospitals, or elsewhere. The program has evolved slowly in that long recommended procedures were postponed far too long. For example, since 1936, when the University Hospital found routine patient admission and personnel examinations so valuable, they were not adopted by the Minneapolis General Hospital until 1938, St. Mary's Hospital in 1952, and Fairview and Swedish in 1953. Some of these institutions were also slow in accepting rigid contagious disease technique.

One of the serious problems was affiliations with other hospitals for brief or long periods of special training, notably institutions for the mentally ill. Many of these situations have so changed that the future protection of student nurses seems reasonably well assured. Not only have their home schools adopted patient entrance and personnel examinations but also through a program initiated and promoted by Dr. H. A. Burns, all institutions for the mentally ill have admission and frequent periodic examinations. Those who on admission or subsequently present definite or suspected tuberculous lesions are promptly transferred to a tuberculosis service of some 400 beds in one institution where good contagious disease technique is practiced. Another encouragement comes from the fact that all general hospitals in Minneapolis and St. Paul have adopted these effective procedures for protection of student and graduate nurses.

We now recommend that for each entering class a large graph be started on which the percentage of reactors on admission in indicated. To this the percentage of reactors is added at the end of each six months test. This promptly brings to the attention of administrators and professional staffs errors or oversights in admission examinations and violations in contagious disease technique. Nothing but the tuberculin test adequately provides such information.

Suggestions and Recommendations of Graduates

In 1952 and 1953, we asked all graduates of the classes from 1930 to 1951 inclusive for suggestions which would provide better protection of student and graduate nurses in hospitals. The response was almost overwhelming. One said, "Let's demand that each patient admitted be carefully examined for tuberculosis." She graduated in 1930 and said that where she has been employed in later years there has been an amazing indifference to safety for nurses. She cited cases admitted to hospitals for surgery whose physicians neglected to inform nurses of coexisting contagious tuberculosis.

One who graduated before our program was well established said, "I feel that conditions at my training school contributed greatly toward my breakdown. I would like very much to see conditions change. As it stands now, I would be very reluctant to allow a daughter of mine to go into

nursing." Another wrote. "Full cooperation of doctors in carrying out isolation technique is a contributing factor." She suggested periodic chest x-ray film inspection every three months for all tuberculin reactors. One said, "Many are negligent in carrying out the contagious disease technique. I have admired the work done in my school of nursing." Another said, "A genuine positive school health program is a necessity. Watch tuberculin reactors especially."

Most suggestions were in the same general vein indicating the desire of nurses to solve their tuberculosis problem. Many wrote of the worthwhileness of the program in their schools to them, not only while students but also through subsequent years.

Present Tuberculosis Status of Graduates

An attempt was made to contact the graduates in the classes from 1930 to 1951 inclusive of the four original study schools to bring their tuberculosis status to date. Of the 4,633 in these classes, 4,030 (87 per cent) were located. Fifty-five had died and complete information pertaining to tuberculin reaction, x-ray films of the chest was not obtained in 65. However, all with incomplete information stated that they have remained in good health. Causes of death of the 55 graduates are as follows:

Accidents	9	Leukemia	3
Addisons (nontuberculous)	1	Lungs (7 tuberculosis)	11
Appendicitis	2	Malignancy	6
Brain conditions	6	Nephritis	1
Cardiovascular	9	Poliomyelitis	2
Childbirth	1	Streptococcus Infection	1
Hepatitis	1	Suicide	2

When the graduates who had died (55), those untraced (603), and those with incomplete information (65) were deducted, there remained 3,910 for present consideration.

Infections Since Graduation

An opinion has been ventured that most nurses who have not been infected before graduation become tuberculin reactors within a few years. Among the 2,441 contacted graduates who were not infected on completion of training, 414 (17.0 per cent) have since acquired infection.

Areas of Disease in Tuberculin Reactors

In the second decade of this century, Ghon demonstrated that persons who react characteristically to tuberculin have lesions, most of which can be located only at necropsy. When the initial infection with tubercle bacilli occurs, regardless of whether organisms enter by way of the digestive tract, respiratory tract, eye, abrasions or punctures in skin, female reproductive tract, or are willfully injected into or beneath the skin or directly into any tissue or even the bloodstream, they are promptly phagocytosed by neutrophils which often carry them about in blood and lymph channels. Within an hour after phagocytosis occurs, tubercle bacilli are focalized in numerous parts of the body. At the points of focalization, tubercles promptly begin to form which may harbor bacilli

over brief or long periods. Thus from the beginning, tuberculosis is a generalized disease.

At first none of these lesions can be found by any phase of an examination. However, in a few weeks the body tissues, including the skin, become sensitized to the protein of tubercle bacilli, after which the presence of these microscopic lesions harboring tubercle bacilli can be detected by testing with tuberculin.

Present methods of examining the human body are not sufficiently refined to detect locations of these initial lesions, as most of them are too small or do not have consistency to cast visible shadows on x-ray film. Since 25 per cent of the lungs is obscured from view by such structures as the heart and diaphragm, and others are located extrathoracically, the usual x-ray film inspection of the chest does not locate lesions in these areas regardless of their size and consistency. Therefore only periodic roentgen inspection of the chest is not a satisfactory procedure.

About the time allergy can first be detected by the tuberculin test the x-ray film of the chest is usually clear. However, in a few, rarely more than 5 to 8 per cent, shadow-casting primary infiltrations are then demonstrable or appear soon after. The majority of such lesions do not become clinical but gradually recede until they disappear from x-ray view. Later, in 25 per cent or less, calcific deposits at the site of the original focus, in the regional lymph nodes or both become large enough to be identified by shadows on x-ray films.

When demonstrable pulmonary lesions appear within three months of the time the individual converts to a tuberculin reactor, they nearly always prove to be primary infiltrates, whereas, lesions which evolve to shadow-casting proportions later usually represent reinfection type of disease. When the time of tuberculin conversion is not known, only the characteristic course of primary infiltrates identifies them. It is important to make this differentiation, inasmuch as primary lesions are initiated in non-allergic tissues, and therefore are usually benign, while reinfections begin to develop in allergic tissues and are likely to become clinical.

Our observations have led us to believe that the majority of clinical lesions are due to endogenous reinfection. Thus, the entire evolution of tuberculosis in a human body starts with focalizations of bacilli within an hour after the invasion occurs. These focalizations are multiple and some are located extrathoracically. At any subsequent time throughout the individual's life as long as tubercle bacilli remain alive, one or more of these areas may release organisms on allergic tissue and result in clinical disease in the immediate vicinity or in more remote parts. Hence, the importance of periodic examination of all nurses, whether the infection occurs before entering school, during training, or subsequently.

Lesions Among Students Who Reacted to Tuberculin on Admission

Among the 4,633* students who graduated from the original four schools of nursing in the classes of 1930 to 1951 inclusive, 758 (16.4 per cent)

*No record of tuberculin test in 34, therefore not traced.

reacted to tuberculin on entrance. Obviously, all possessed multiple tuberculous lesions despite good general health and clarity of chest x-ray films. Sixteen per cent presented evidence of parenchymal or hilum region calcific deposits. It is likely that some of these deposits were due to such conditions as fungus infections. However, among the 3,841 who entered as nonreactors to tuberculin, only 2 per cent had evidence of calcific deposits. Therefore, it seems probable that 14 per cent of the calcium deposits in the reactors were in the vicinity of tuberculous lesions. Similar observations have been made on students of medicine and sizeable groups of children.

Inasmuch as students who had previously been infected, some of whom had allergic manifestations about the time allergy was well established, including demonstrable primary pulmonary infiltrates, erythema nodosum, pleurisy with effusion, etc., lesions which evolved while in school or subsequently were of the reinfection type. Among those who had been infected before entering school, the following presented clinical disease before graduation. One had a pulmonary lesion appear in her freshman year (1932), which was treated. She later graduated and has been well since. One presented a pulmonary lesion (1934) which was treated successfully and she has remained in good health. One who had a pulmonary lesion appear in her senior year (1935) has been well since treatment. One who had a pulmonary lesion appear in 1945 was treated by ambulatory artificial pneumothorax and has worked continuously for the past 10 years. One was treated by artificial pneumothorax and was in a sanatorium for 16 months (1947). She has been in good health for the succeeding six years. Another had slight x-ray film changes appear around an old calcified focus (1949). She was hospitalized one year but the disease did not become clinical and tubercle bacilli were not recovered. One had a pulmonary lesion appear in 1951. She was hospitalized nine months and has since been in good health. Within *one year* after graduation, one had pleurisy with effusion. She has had no further development in the past 16 years. Another was hospitalized for pulmonary tuberculosis with good apparent recovery (1939). Seven years later the lesion reactivated but came under control. In 1954, there was evidence of cavitation in the old lesion which was resected in 1955.

Two years after completing training one presented a pulmonary lesion which was treated and she has been well for the past 18 years.

Three years after graduation one had pulmonary tuberculosis which responded to treatment. She has been in good health for the last 21 years. Another was hospitalized for pulmonary disease. She made good recovery and has been well for eight years.

Four years after finishing training one presented a lesion in the upper lobe of the left lung (1934). Thoracoplasty was done in 1939. She has been in good health since convalescence.

Five years after graduation one had a pulmonary lesion which was controlled. She has remained well for the last seven years. Another developed

tuberculosis of the second and third lumbar vertebrae (1939). The spine was fused and she returned to work in 1939. In 1948 the left trochanteric bursa and the greater trochanter of the femur were involved. Following surgery she has remained apparently well. One died from pulmonary tuberculosis (1938).

Six years after graduation one had pulmonary tuberculosis which was successfully treated and she has been well over the past 15 years. Another died from pulmonary tuberculosis (1937).

Seven years later one presented a pulmonary lesion from which she recovered and has been in good health for the past 16 years. One died from pulmonary tuberculosis (1941).

In the *eighth year* one was treated for pulmonary tuberculosis in a sanatorium (1941). No further evidence of disease has appeared in the succeeding 13 years.

In the *11th year* one developed pulmonary disease and died from tuberculosis in a sanatorium in 1943.

In the *13th year* two from the class of 1932 developed pulmonary tuberculosis. Their lesions were found in 1945. One had lobectomy in 1952. The other died in 1946 from extensive pulmonary disease, laryngitis, and enterocolitis.

In the *19th year* one had pulmonary disease and was treated with pneumoperitoneum. She has remained well for the past two years.

Thus, among 758 students who were harboring tubercle bacilli on entrance to schools of nursing, 26 (3.4 per cent) have developed tuberculosis which was treated. Five have died.

Lesions Among Those Who Became Infected While in School

Among the 3,841 who began training uninfected, 950 (24.7 per cent) were infected while in school. Although all had multiple tuberculous lesions, in only the following were they located. Twelve presented primary pulmonary infiltrates. None of the 12 has had subsequent tuberculous developments over the four to 25 years since graduation.

Seven developed pleurisy with effusion while in school. All have remained well over the subsequent 12 to 28 years except one who soon presented bilateral tuberculosis and required sanatorium treatment. She made good recovery.

Two students had demonstrable primary pulmonary infiltrates in evidence when pleural effusion appeared. One has remained well over the past 22 years. The other had the infiltrate resected in 1951 and has been well since convalescence.

One developed a reinfection type of pulmonary lesion one year after she was infected. This was treated successfully and she completed training. However, she died from tuberculous pneumonia five years later (1936). Another had bilateral pulmonary lesions requiring sanatorium treatment. She has been well for the past 19 years.

During the *first year* after graduation one had pleurisy with effusion. She has had no further trouble for the past 14 years. Another developed

a pulmonary lesion which required treatment. She has been well for the succeeding 21 years. One presented a pulmonary lesion which required treatment. There has been no recurrence over the past 10 years.

In the *second year* six developed demonstrable lesions. One had pleurisy with effusion and was hospitalized 14 months. No further development has occurred in the succeeding eight years. One was hospitalized nine months for a pulmonary lesion with no recurrence over the succeeding 14 years. One had thoracoplasty with no recurrence for the past 14 years. One had a minimal lesion which was treated in 1941. She has since been in good health. One was treated by ambulatory artificial pneumothorax (1936). She recovered but died in 1945 from leukemia. One had a minimal lesion for which she was hospitalized. She has been well for the past 28 years.

During the *third year* one developed a pulmonary lesion and pleural effusion. She was treated in a sanatorium (1948). The lesion reactivated in 1954 and she was discharged in 1955. Four others presented pulmonary lesions. One was treated by ambulatory pneumothorax and has been well the past 20 years. Two were hospitalized for pulmonary lesions. They have had no recurrence during the past 15 years. The fourth was also hospitalized. She has been well during the succeeding nine years.

In the *fourth year* one developed pleurisy with effusion. She has remained well for the succeeding five years. Four developed pulmonary lesions. One was hospitalized but there has been no recurrence during the succeeding 18 years. Another who was hospitalized has had no recurrence for the past eight years. One who was hospitalized in 1951 made good recovery. The fourth was treated by ambulatory artificial pneumothorax. She has been well for the past five years.

During the *fifth year* one presented a minimal pulmonary lesion which was treated by ambulatory artificial pneumothorax. She has been well for the past five years. Another was hospitalized for a pulmonary lesion. She has been well for the past 12 years.

In the *seventh year* one developed a pulmonary lesion which was treated in the home. She has remained well during the succeeding five years.

In the *eighth year* one had pleurisy with effusion (1948) and was hospitalized 12 months. In 1954 she had extensive pelvic tuberculosis which was treated surgically.

During the *ninth year* one was institutionalized for pleurisy with effusion. She has been well the succeeding 13 years.

In the *10th year* one had tuberculosis of cervical lymph nodes which required treatment. Another had a minimal pulmonary lesion evolve for which she was hospitalized. Five years later a lesion appeared in the contralateral lung which responded to treatment. She has been in good health for the past five years.

During the *12th year* one had bilateral pulmonary tuberculosis (1943) which required hospitalization and resection. She has made good recovery.

In the *15th year* one developed a pulmonary lesion for which she was hospitalized in 1953.

In the *18th year* one had pleurisy with effusion (1951) for which she was treated in a sanatorium for one year. She has since remained well.

Thus, among 950 students who acquired primary tuberculosis while in school, 21 had demonstrable allergic manifestations consisting of primary infiltrates and pleurisy with effusion. Thirty-one (3.3 per cent) presented reinfection type of tuberculosis, of whom one died from tuberculous pneumonia five years after infection occurred.

Of the 29 known to have developed clinical tuberculous lesions after graduation, nine had them appear within two years after graduation, five in three and five in four years. The remaining 10 were quite evenly distributed over the next 17 years.

Lesions Among Those Who Became Infected After Graduation

Among the 2,441 contacted nurses who were uninfected at the time of graduation, 414 (17.0 per cent) have acquired primary tuberculosis. Demonstrable lesions presented themselves in the following. During the *first year* after graduation, one had a demonstrable primary infiltrate for which she was hospitalized one year. She has remained well for the succeeding four years. Another presented a primary infiltrate which was treated by artificial pneumothorax in a sanatorium. She has been well for the past nine years. One had a primary infiltrate and pleural effusion in 1944. In 1950 a small reinfection type of lesion appeared and she was hospitalized for eight months. She has been well since. One who presented a primary infiltrate had no treatment. She has been well over the succeeding 20 years. Another was hospitalized for a primary infiltrate. She has been in good health for the past 23 years.

One who was infected the *first year* after graduation presented a pulmonary lesion two years later. She responded to treatment and has been well for the past seven years. One was hospitalized for a pulmonary lesion which was resected. She has been well for the succeeding nine years. Another who became infected in 1946 presented a pulmonary lesion in 1948 which responded to treatment in a hospital. She is now in good health. One infected in 1945 developed a pulmonary lesion in 1948. This was controlled by artificial pneumothorax.

During the *second year* one developed pleurisy with effusion and was treated in a sanatorium. She has been well for the succeeding nine years.

Another infected in 1949 was hospitalized one year for pleurisy with effusion. In 1953 she had tuberculous peritonitis and was hospitalized for 17 months. Another infected in 1947 was hospitalized in 1949 for a right apical lesion which was resected. She has been well for the past four years.

During the *third year* one presented a primary pulmonary infiltrate which was treated in a sanatorium with artificial pneumothorax. She has been well for the past four years. Another had a demonstrable primary infiltrate for which she was hospitalized and the lesion was resected in 1954. One had pleurisy with effusion and was hospitalized three months. She has been in good health for the past 12 years.

In the *fourth year* one presented a primary infiltrate which was treated by artificial pneumothorax. She has remained well during the succeeding 12 years. Another had a primary infiltrate which was not treated. She has been well for the past nine years. One had a primary infiltrate (1952) which was resected. One had pleurisy with effusion (1936). She was out of work one year and has been well since. One developed pulmonary disease which was brought under control. However, lesions reactivated eight years later and were treated successfully.

During the *fifth year* one developed a minimal pulmonary lesion two years after infection. This did not become clinical and she has been in good health for the succeeding 17 years. One who graduated as a non-reactor to tuberculin in 1937 died in a sanatorium from pulmonary tuberculosis in 1942. Her sanatorium record has been destroyed and we have no information as to where and when her infection was acquired. One infected in 1940 had pleurisy with effusion and was treated six months. She has been well since.

During the *sixth year* one presented a primary infiltrate and pleural effusion. She was hospitalized 16 months and has remained well over the succeeding 14 years.

In the *seventh year* one presented a primary infiltrate (1953). She was hospitalized one year and the lesion was resected.

During the *eighth year* one was infected and presented a pulmonary lesion eight years later. She has been in good health the past six years.

In the *11th year* one developed a pulmonary lesion (1941). She was institutionalized and had artificial pneumothorax. She is now in good health.

In the *14th year* one had a diagnosis of bilateral pulmonary sarcoidosis (1944) for which she was in a sanatorium two months and again briefly in 1946. In 1948 she had become a reactor to tuberculin and a diagnosis of pulmonary tuberculosis was made. She was again in a sanatorium for 17 months and one year later for 12 months. The disease has been considered inactive for the past five years.

In the *15th year* one developed endobronchial tuberculosis without evidence of pulmonary disease (1953). She was hospitalized for nine months and is still on chemotherapy.

During the *20th year* one presented a primary infiltrate and was hospitalized for six months. She has remained in good health for the succeeding five years.

One who graduated in 1931 was last tested with tuberculin in 1929 when she did not react. She had no subsequent test because she "does not believe in tuberculin tests." She worked in sanatoriums and in 1948 was found to have pulmonary tuberculosis for which she was hospitalized 22 months and had artificial pneumothorax for three and one half years.

Thus, among 2,441 who graduated uninfected, 414 have acquired primary tuberculosis. Nineteen presented demonstrable allergic manifestations, such as primary pulmonary infiltrates and pleurisy with effusion about the time allergy was established. All have remained in good health

except one who later had tuberculous peritonitis and one a minimal pulmonary lesion. In addition to the last two, 13 others, a total of 15 (3.7 per cent) have had clinical tuberculosis. One died.

Classification of Lesions

The demonstrable lesions which these students and graduates presented could lead to erroneous deductions if they were not classified. They must be divided into two main groups and kept separate: 1. Consists of lesions (primary infiltrates) resulting from the original invasion with tubercle bacilli. They are present in all persons who react characteristically to tuberculin. A few primary infiltrates become large enough and have such consistency as to obstruct x-rays. About the time allergy is in evidence, the occasional primary lesion, whether or not it is visualized on the x-ray film, involves the pleura and pleurisy with effusion appears. This is usually regarded as an allergic reaction. 2. Lesions which evolve months, years, or decades after allergy has been established. These are due to reinfections which probably are mostly endogenous and constitute practically all progressive clinical tuberculosis.

The 758 students who entered school as tuberculin reactors had developed multiple primary lesions soon after they were infected, but only approximately 14 per cent of them presented demonstrable residuals on entrance to school. The 1,364 who became infected while in school or after graduation had the same evolutionary development of lesions, the only difference being that they occurred later in the lives of these individuals and therefore primary infiltrates or pleurisy with effusion appeared in some of them just as had occurred earlier in life in some who were infected before entering school. These conditions are in no way comparable to the reinfection type of lesions which later developed among those who entered already infected and those who subsequently became infected.

Treatment

The successful treatment of students and graduates who developed clinical tuberculosis, has been in considerable part due to early diagnosis. Those who reacted to tuberculin on entrance and others who became reactors as students were examined semiannually until graduation. In contacting the graduates, it was gratifying to learn that many had followed the program in which they had participated while in school. Chronic pulmonary tuberculosis evolves slowly and if reactors are examined with sufficient frequency, lesions destined to develop can nearly always be found in the pre-symptom and pre-contagious stage, and when they can be treated successfully. Exceptions are acute exudative lesions, meningitis, and miliary disease which strike suddenly.

Thus, in the pre-antimicrobial drug and resectional surgery era, most of our students and graduates recovered. In fact, there have been only seven deaths among those contacted in the classes of 1930 to 1951 inclusive. Five were infected before entering school, one of whom died in 1937, one

in 1938, one in 1941, one in 1943, and one in 1946. One who was infected in school (1931) died in 1936 and one infected after graduation died in 1942.

One cannot determine severity of disease among our graduates from the treatment they have received. They are widely scattered throughout this country and in a number of other nations. Methods of treatment employed by physicians in different areas vary greatly. For example, in some areas minimal clinical lesions have been treated by artificial pneumothorax and in more recent years by resection. This even applies to primary infiltrates.

Today many recent tuberculin converts are receiving antimicrobial drugs. Numerous physicians believe this is the only opportunity one has to treat tuberculosis with the hope of effecting a cure in the strict sense of the word. In recent converters, the multiple lesions are usually microscopical and vascular. Drugs may be expected to reach all tubercle bacilli, whereas if one waits until lesions have lost vascularity, there is little hope of destroying all tubercle bacilli.

It is not known whether present drugs, even though they contact all tubercle bacilli in recent converters, are capable of destroying the organisms. Unquestionably, they markedly suppress tubercle bacilli and evidence is accruing to show that prompt treatment of recent converters at least prevents acute destructive forms of tuberculosis such as meningitis and generalized miliary disease. If even this proves as effective as it now appears, it makes the earliest possible diagnosis of tuberculosis mandatory. This can be made only with the tuberculin test.

Inasmuch as recent converters usually have neither x-ray shadows nor symptoms, the only criterion for discontinuing treatment is the loss of sensitivity to tuberculin. This has actually occurred in a few persons, including nurses, who have been treated by antimicrobial drugs immediately after tuberculin conversion. However, it is still a question as to whether tubercle bacilli have been destroyed or only suppressed to such low level that they are not proliferating and therefore are not eliminating tuberculoprotein which is necessary to maintain sensitivity of tissues.

Experimental workers have revealed that animals highly susceptible to tubercle bacilli, when given antimicrobial drugs regularly before and during exposure to tuberculous animals do not develop tuberculosis. The drugs are already in the body when tubercle bacilli enter and apparently prevent them from gaining footholds. If further work proves that tuberculous lesions can be prevented from forming in this manner, this procedure may be of great value to student and graduate nurses under certain difficult situations, such as those who care for uncooperative and tuberculous mentally ill individuals.

Although we are now treating a small number of recent tuberculin converters with antimicrobial drugs and two have reverted, the period of observation is far too short and the number of cases too limited to justify deductions.

SUMMARY AND CONCLUSIONS

1. This study, undertaken in schools of nursing in 1920, at first consisted of examining and treating students who presented symptoms. In 1927, an attack was begun on the tubercle bacillus rather than just the damage it had caused. This consisted of testing students with tuberculin, thus dividing them into two groups: (a) Reactors who were harboring tubercle bacilli, and (b) those who were uninfected.

2. Reactors on entrance were examined semiannually while in school. Students uninfected on entrance were retested semiannually and converters were examined every six months.

3. Periodic examinations of tuberculin reactors usually revealed clinical lesions while in the silent stage, before they were contagious and when treatment was successful.

4. Periodic testing of the uninfected on entrance provided the earliest possible diagnosis of tuberculosis. Moreover, it served as an excellent epidemiological agent.

5. Sources of infections of converters were sought. This led to affiliated hospitals, sanatoriums, departments within the home schools, etc. Finding such offenders was reason to discontinue or correct them.

6. In one school, patient admission and personnel examinations were conducted as a demonstration in 1933. In 1936 and in 1938 this was made routine in two other schools and in the remaining institutions in 1952 and 1953.

7. Investigation of all methods of protecting students that have been proposed revealed only one that seemed sound, namely, management of tuberculosis as a contagious disease.

8. Contagious disease technique was instituted in one school in the early 1930's and proved so adequate that it is now employed in most general hospitals of this area. Periodic testing with tuberculin is the best criterion as to whether technique is being rigidly enforced.

9. Infection with tubercle bacilli may cause not only early illness such as pleural effusion but also and more often serious tuberculosis years and decades later. A tuberculin reaction is an ill omen as it is the first manifestation of the presence of tuberculosis. Student and graduate nurses are justified in demanding adequate protection whenever and wherever they are in contact with contagious cases of tuberculosis.

10. In the four original study schools, 5,304 students graduated in the classes from 1930 to 1954 inclusive, of whom 807 (15.2 per cent) had been infected before admission. Among the remaining 4,497, infections were acquired by 1,020 (22.7 per cent) students. In the classes from 1930 to 1942, of the 1,619 who entered uninfected, 575 (35.5 per cent) converted. In the classes from 1943 to 1949, of the 1,876 uninfected on entrance, 324 (17.3 per cent) converted. After 1949 there were 1,002 nonreactors, of whom 121 (12.1 per cent) converted. Obviously, the tuberculin conversion problem has not been completely solved, but it appears the methods now in use are capable of doing so.

11. All persons who react characteristically to tuberculin have at least

multiple primary lesions. Therefore, in the classes of 1930 to 1954, the 807 students who reacted on entrance had such lesions. Among the 758 in the classes from 1930 to 1951, reinfection type clinical lesions evolved in 26 (3.4 per cent), seven while they were in school and 19 after graduation. Five died.

12. Among the 950 (classes of 1930 to 1951) who converted while in school, all of whom had primary lesions, clinical tuberculosis appeared in 31 (3.3 per cent), two in students and 29 since graduation. One died.

13. Among the 2,441 uninfected on graduation who were contacted, 414 have converted. Of this number, 15 (3.6 per cent) have had clinical tuberculosis. One died.

14. To avoid erroneous deductions, tuberculous lesions must be classified. Demonstrable allergic manifestations, including erythema nodosum, primary pulmonary infiltrates and pleurisy with effusion, which appear about the time allergy is established, belong to the same category as other lesions which are too small or are not so situated as to be detectable but are present in all tuberculin reactors. The only difference is consistency, position and size. They are in no way comparable to reinfection clinical type lesions which later evolve.

15. With decreased incidence of infection there has been a corresponding reduced number of clinical lesions. In the classes of 1947 through 1951, only seven are known to have developed clinical disease, five of whom were in classes of 1947. In the Fairview School, where 12 to 19 per cent developed demonstrable lesions before protective measures were well under way, there have since been only four students, who, while in school, developed clinical pulmonary tuberculosis. All four were infected before admission to school.

16. Many nurses who finished training uninfected with tubercle bacilli have traveled and worked in various other parts of this country and abroad, including military service, where contagious tuberculosis is rife, but we have seen no evidence to substantiate the theory that those who acquired infections later in life tolerated them differently than those infected in childhood or as students.

17. Treatment of tuberculosis among student and graduate nurses included in this study has been that in vogue at the time demonstrable lesions evolved. With antimicrobial drugs, it may be possible to effect a cure if administered promptly after invasions with tubercle bacilli occur. The lesions are then small and vascular and drugs may be expected to reach all bacilli. If present or future drugs prove to be germicidal, one may hope to destroy all organisms at that time. More observation is necessary before final conclusions can be drawn concerning efficacy of such treatment.

18. In this study, the tuberculin test has been the master key. It detects presence of tuberculosis earlier than any other procedure, is our best epidemiological agent, best determines magnitude of problem, provides best evidence of effectiveness of control measures and now may determine not only when to begin but also when to stop treatment.

RESUMEN Y CONCLUSIONES

1. Este estudio emprendido en las escuelas de enfermería en 1920 primeramente consistió en el examen y trataminto de las estudiantes que presentaron síntomas. En 1927 se inició un ataque hacia el bacilo más bien que hacia el mal que él producía. Consistió esto en hacer las pruebas de tuberculina dividiéndolas en dos grupos: (a) reactores que tenían en su organismo el bacilo de la tuberculosis y (b) los no infectados.

2. Las reactoras eran examinadas semestralmente mientras estaban en la escuela. Las estudiantes no infectadas al ingreso eran sometidas a las pruebas tuberculínicas semianualmente y las que virabanse examinaban cada seis meses.

3. Los exámenes periódicos de los reactores a la tuberculina generalmente revelaban lesiones clínicas en una etapa silenciosa, antes de ser contagiosas y cuando el tratamiento era más eficaz.

4. La prueba periódica de las no infectadas al ingreso proveyó el diagnóstico más temprano posible de la tuberculosis. Más aún, sirvió como un excelente medio de estudio epidemiológico.

5. Se buscaron las fuentes de infección de las que viraban. Esto se llevó hacia los hospitales afiliados, sanatorios, departamentos dentro de las escuelas hogares, etc. Encontrando tales fuentes se justificaba la suspensión o corrección de ellas.

6. En una escuela, la admisión de enfermos y los exámenes del personal se condujeron como una demostración en 1933. En 1936 y en 1938 esto se hizo de manera rutinaria en otras dos escuelas y en el resto de las instituciones en 1952 y en 1953.

7. La investigación de todos los métodos para proteger a los estudiantes que se había propuesto reveló que había sólo uno que parecía apropiado: el cuidado de la tuberculosis como una enfermedad contagiosa.

8. La técnica de las enfermedades contagiosas se instituyó en una escuela al principio de los años después de 1930 y se mostró tan adecuada que ahora es empleada en la mayoría de los hospitales en esta región. La prueba periódica de la tuberculina es el criterio mejor respecto de la técnica que debe emplearse.

9. La infección por el bacilo tuberculoso puede no sólo causar una enfermedad inmediata tal como derrame pleural sino también y más a menudo, tuberculosis severa años y décadas más tarde. Una reacción positiva de tuberculina es un mal indicio ya que es la primera manifestación de la presencia de tuberculosis. Los estudiantes y las enfermeras graduadas tienen razón al demandar una protección adecuada cuando y donde ellos están en contacto con casos contagiosos de tuberculosis.

10. En los cuatro estudios originales de escuelas, 5,304 estudiantes graduadas en las clases de 1930 a 1954 inclusive, de las que 807 (15.2 por ciento) se habían infectado de tuberculosis.

Entre el resto: 4.497, se adquirieron infecciones por 1.020 (22.7 por ciento) estudiantes. En las clases de 1930 a 1942, de 1.619 que ingresaron no infectadas, 575 (35.5 por ciento) viraron a positivas. En las clases de 1943 a 1949, de 1.876 no infectadas al ingreso, 324 (17.3 por ciento) vira-

ron. Después de 1949 hubo 1.002 no reactoras de las que 121 (12.3 por ciento) viraron.

Es evidente que el problema del viraje de la tuberculina no ha sido resuelto pero parece que el método en uso hoy es capaz de lograrlo.

11. Todas las personas que reaccionaron característicamente a la tuberculina tenían por lo menos múltiples lesiones primarias. Portanto en las clases de 1930 a 1954, los 807 estudiantes que reaccionaron a la entrada tenían tales lesiones. Entre las 758 en las clases de 1930 a 1951, las lesiones de tipo clínico de reinfección aparecieron en 26 (3.4 por ciento), siete mientras estaban en la escuela y 19 después de graduadas. Cinco murieron.

12. Entre las 950 (clases de 1930 a 1951) que viraron mientras estaban en la escuela, todas las cuales tuvieron lesiones primarias, apareció tuberculosis clínica en 31 (3.3 por ciento), dos en estudiantes y 29 después de la graduación. Una murió.

13. Entre las 2.441 no infectadas al tiempo de graduarse, que después fueron puestas en contacto, 414 viraron. De este número, 15 (3.6 por ciento) tuvieron tuberculosis clínica. Una murió.

14. Para evitar deducciones erróneas, las lesiones tuberculosas deben clasificarse. Las lesiones alérgicas demostrables, incluyendo el eritema nudoso, infiltrados pulmonares primarios y pleuresía con derrame que aparecen alrededor del tiempo del establecimiento de la alergia, pertenecen a la misma categor a que las otras lesiones que son muy pequeñas o no están consideradas como descubribles pero que existen en todos los reactores a la tuberculina. La única diferencia es la consistencia, situación y tamaño. No son comparables en modo alguno el tipo clínico de la tuberculosis de reinfección que más tarde aparece.

15. Con el decrecimiento de la incidencia de la infección ha habido un número decreciente también de lesiones clínicas. En las clases de 1947 hasta 1951 sólo se sabe de 7 que se presentaron como enfermedad clínica, cinco de las cuales fueron del grupo de 1947. En la escuela de Fairview, donde 12 a 19 por ciento desarrollaron lesiones demostrables antes de que se tomaran medidas de protección, ha habido sólo 4 estudiantes que durante su estancia en la escuela desarrollaron tuberculosis pulmonar clínica.

Las cuatro se habían infectado antes de su entrada a la escuela.

16. Muchas enfermeras que terminaron su educacion no infectadas por el bacilo tuberculoso han viajado y trabajado en otros lugares del País y afuera de él, incluyendo el servicio militar en donde la tuberculosis prospera, pero no se ha visto evidencia en favor de la idea de que los que adquieren la infección tarde en la vida, toleren la infección de modo diferente de los infectados en la infancia o como estudiantes.

17. El tratamiento de la tuberculosis entre las estudiantes y enfermeras graduadas en este estudio, sa sido puesto práctica en el momento que aparecieron lesiones demostrables. Con las drogas antimicrobianas, puede ser posible efectuar una curación si se administran inmediatamente después de la invasión por el bacilo. Las lesiones son entonces pequeñas y vasculares y las drogas se espera que alcancen a todos los bacilos.

Si las actuales o las futuras drogas demuestran ser germicidas, puede uno

esperar destruir tos o los gérmenes en esa etapa. Se necesita más observación antes de llegar a conclusiones finales respecto de la eficacia de este tratamiento.

18. En este estudio la prueba tuberculínica ha sido la llave maestra. Descubre la presencia de la tuberculosis más temprano que cualquier otro procedimiento, es nuestro agente epidemiológico mejor, el que determina mejor la magnitud del problema, da mejor evidencia de la efectividad de las medidas de control y ahora puede determinar no sólo cuando empezar sino cuando terminar el tratamiento.

RESUME

1. Cette étude entreprise dans les écoles d'infirmières en 1920 consista d'abord à examiner et traiter les étudiantes qui présentaient des symptômes. En 1927, l'attaque fut dirigée contre le bacille tuberculeux lui-même plutôt que contre les troubles dont il était responsable. Cela consista à rechercher les tests à la tuberculine, puis à séparer les étudiantes en deux groupes: a) celles qui réagissaient à la tuberculine et avaient donc été parasitées par le bacille, b) celles qui n'avaient pas été parasitées.

2. Celles qui avaient des réactions tuberculiniques positives à leur entrée furent examinées deux fois par an pendant leur stage à l'école. Les étudiantes indemnes à l'entrée, avaient de nouvelles réactions tuberculiniques deux fois par an, et celles qui viraient leur cuti-réaction étaient examinées tous les six mois.

3. Les examens péridiques des étudiantes à cuti-réaction positive révélèrent généralement des lésions cliniques alors qu'elles étaient encore silencieuses, avant qu'elles ne soient contagieuses, et lorsque le traitement avait toutes les chances d'être couronné de succès.

4. Les tests périodiques des porteurs de cuti-réactions négatives à l'entrée assura le diagnostic le plus précoce possible de la tuberculose. De plus, ils se révélèrent un excellent procédé épidémiologique.

5. Les sources d'infections de ceux qui avaient viré leur cuti-réactions furent cherchées. Ceci conduisit aux hôpitaux affiliés, sanatoriums, services faisant partie des écoles. La découverte des responsables permit de les écarter ou de les traiter.

6. Dans une école, en 1933, l'admission des malades et les examens du personnel furent exécutés à titre expérimental. En 1936 et en 1938, ceci devint la routine de deux autres écoles, et dans le reste des institutions en 1952 et 1953.

7. L'examen de toutes les méthodes de protection des étudiantes qui ont été proposées, révéla que la seule qui semblait valable était celle qui proposait que l'on considère la tuberculose comme une maladie contagieuse.

8. Les dispositions concernant les maladies contagieuses furent appliquées dans une seule école, dans les premières années qui suivirent 1930, et elles révélèrent si fructueuses que maintenant elles sont employées dans la plupart des hôpitaux généraux de cette région. Le test périodique à la tuuberculine est le meilleur critère pour indiquer que les dispositions

sont appliquées d'une façon stricte.

9. L'infection par le bacille tuberculeux peut occasionner non seulement une atteinte immédiate, telle que l'épanchement pleural, mais aussi et plus souvent, une tuberculose sérieuse des années et des décades après. Une réaction tuberculinique positive est une mauvaise éventualité, car c'est la première manifestation de la présence de tuberculose. Les étudiants et les infirmières diplômées peuvent légitimement demander une protection adéquate là où ils sont en contact avec des cas de tuberculose contagieuse.

10. Dans les quatre centres originels, 5.034 étudiantes furent diplômées dans les classes de 1930 à 1954 inclusivement, parmi lesquelles 807 (15,2%) étaient infectées avant leur admission. Parmi le reste des étudiantes (4.497), 1.020 étudiantes furent infectées (22,7%). Dans les classes de 1930 à 1942, sur les 1.619 étudiantes qui furent admises avec une cutiréaction négative, 575 (35,5%) virèrent leur réaction. Dans les classes de 1943 à 1949, sur les 1.876 porteurs de cuti-réactions négatives à l'entrée, 324 (17,3%) effectuèrent leur virage. Après 1949, il y eut 1.002 étudiantes à cuti-réaction négative, dont 121 (12,2%) virèrent. Evidemment, le problème du virage tuberculinique n'a pas été complètement résolu, mais il apparait que les méthodes actuellement utilisées sont capables de le faire.

11. Toutes les personnes qui réagissent à la tuberculine ont au moins des lésions primaires multiples. C'est pourquoi, dans les classes de 1930 à 1954, les 807 étudiantes qui réagirent à leur entrée avaient de telles lésions. Parmi les 758 étudiantes dans les classes de 1930 à 1951, des lésions cliniques à type de réinfection évoluèrent chez 26 (3.4%) sept pendant qu'elles étaient à l'école, 19 après leur diplôme. Cinq décédèrent.

12. Parmi les 950 (classes de 1930 à 1951) qui virèrent leur cuti-réaction alors qu'elles étaient à l'école, dont toutes furent atteintes de lésions primaires, une tuberculose clinique apparut chez 31 (3,3%) d'entre elles, deux cas chez les étudiantes, les 29 autres depuis le diplôme. L'une mourut.

13. Sur les 2.441 porteurs de cuti-réactions négatives, 414 ont viré leur réaction. Dans ce nombre, 15 (3,6%) présentèrent une tuberculose clinique. Il y eut un décès.

14. Pour éviter des déductions erronnées, les lésions tuberculeuses doivent être classées. Les manifestations allergiques apparentes, y compris l'érythème noueux, les infiltrats pulmonaires primaires, et la pleurésie avec épanchement, qui apparaissent au moment où l'allergie s'établit, appartiennent à la même catégorie que les autres lésions qui sont trop petites ou ne sont pas situées de façon à être visibles, mais sont présentes chez tout allergique. La seule différence en est l'importance, le siège et la dimension. Elles ne sont en aucun cas comparables aux lésions du type clinique de réinfection qui évoluent plus tard.

15. Avec la fréquence décroissante de l'infection, il y a eu un nombre réduit correspondant de lésions cliniques. Dans les classes de 1947 à 1951, ou connait seulement sept cas qui ont été atteints d'une affection cliniquement décelable, cinq d'entre eux dans les classes de 1947. Dans l'Ecole de Fairview où l'on trouvait toujours de 12 à 19% de lésions visibles qui

se développaient avant les mesures de protection, il y eut seulement 4 étudiantes qui, pendant l'école, eurent une tuberculose pulmonaire. Toutes les quatre avaient été infectées avant leur entrée à l'école.

16. Beaucoup d'infirmières, qui finirent leur stage sans avoir été contaminées par le bacille tuberculeux, ont voyagé et travaillé dans différentes autres parties de cette région et au loin, y compris l'activité militaire, avec des risques fréquents de se trouver exposées à la contagion tuberculeuse. Aucun argument permettant d'alimenter la théorie selon laquelle ceux qui sont contaminés lorsqu'ils sont plus âgés toléreraient la maladie différemment de ceux qui sont contaminés pendant leur enfance ou l'âge scolaire, ne nous est apparu.

17. Le traitement de la tuberculose parmi les étudiantes et les infirmières diplômées compris dans cette étude, a été le traitement habituel des lésions évolutives. Grâce aux produits antimicrobiens, on peut effectuer une cure tout de suite après l'apparition de l'infection tuberculeuse. Les lésions alors sont petites et vascularisées, et les médications peuvent atteindre tous les bacilles. Si les produits actuels ou futurs font la preuve qu'ils sont germicides, on peut espérer détruire tous les microbes en même temps. On doit attendre un plus grand nombre d'observations avant de tirer des conclusions en ce qui concerne l'efficacité d'un tel traitement.

18. Dans cette étude, le test tuberculinique a été la clé de toutes les observations. Il décèle la présence de tuberculose plus précocément que tout autre procédé, il est notre meilleur agent épidémiologique, il détermine le mieux l'amplitude du problème, met le mieux en évidence l'efficacité des moyens de contrôle, et maintenant peut déterminer non seulement quand il faut commencer le traitement mais aussi quand il faut l'arrêter.

Surgical Treatment of Bullous Emphysema

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Bullous emphysema becomes a clinical entity when patients with chronic hypertrophic emphysema, of a localized or generalized form, develop air-cysts that are demonstrable roentgenographically. These air-cysts are generally divided into two types,[6, 14] bullae and blebs, depending on their anatomical relationships to the lung.

Two clinical types of bullous emphysema are encountered and a careful differentiation between them is of utmost importance in assaying the results of surgical management. The first we refer to as Type I or the localized type. The pathology encountered in this type is that of hypertrophic emphysema but it is characterized by its limitation to a lobe, or more specifically to one or more segments or subsegments of a lobe. Such changes may be confined to one lung or may be present bilaterally. It should be emphasized that Type I bullous emphysema is not associated with generalized hypertrophic emphysema and it should be carefully excluded from Type II or the generalized type of bullous emphysema, in which blebs and bullae are encountered as part of a diffuse, bilateral hypertrophic emphysema. Since surgical treatment of the Type I bullous emphysema is rather clear-cut and results are uniformly excellent, it is with Type II bullous emphysema that the remainder of this discussion will be primarily concerned. It is worthy of note that, from the surgical standpoint, Type I bullous emphysema is a clinical separate entity and should not be confused with congenital anepithelial or nonepithelialized cysts.[19]

Evaluation of the Emphysema Patient

In the preoperative evaluation of the emphysema patient certain basic factors arise that are of utmost importance in determining probable results of surgical treatment. These are: (1) degree of involvement; (2) degree of infirmity; and (3) associated conditions.

Degree of involvement can usually be accurately determined by careful study of roentgenograms. Some authors[2, 4] employ angiocardiography to outline the pulmonary vascular bed and consider this an important adjuvant in ascertaining the degree of involvement. Laminagraphic sections[5] are useful to outline atelectatic segments or lobes against the mediastinum and bronchography is useful in studying the bronchial patterns and ruling out the presence of bronchiectasis.

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The degree of infirmity parallels the degree of involvement in most instances. Careful history and physical examination are imperative and frequently lead to near accurate evaluation of the patient before radiographic, cardiologic and respiratory function studies are performed. Fluoroscopic examination is important and the experienced fluoroscopist is frequently able to predict differential ventilatory function, tidal volume and vital capacity with a fair degree of accuracy.[9] Careful attention to the vascular pattern will usually disclose oligemia in the more involved areas and a prominent pulmonary artery and its branches leads to a suspicion of pulmonary hypertension and cor pulmonale.

Pulmonary function studies are invaluable in determining both degree of involvement and infirmity and should include, simple spirometric examinations, maximum breathing determinations and differential bronchospirometry. Estimations of residual lung volume and gas analysis of blood and alveolar air contribute immeasurably to our evaluation when facilities for their measurement are available. Electrocardiographic examination and evaluation by a competent cardiologist are mandatory.

As to associated conditions, asthma, chronic bronchitis and cor pulmonale are the most prominent. Bronchial asthma frequently accompanies emphysema and contributes materially to the infirmity during periods of relapse. Diagnosis of asthma is usually evident from history but if doubt exists one can readily make the diagnosis by employing bronchodilating drugs and performing maximum breathing capacity determinations. An increase in the maximum breathing capacity of 10 per cent or more with the use of bronchodilators is diagnostic of an associated asthmatic component.

Chronic bronchitis in any degree of severity and duration is one of the most serious accompaniments of pulmonary emphysema. Its presence usually portends an objective and subjective failure to any form of surgical treatment.

Presence of cor pulmonale reflects progressive structural changes in the lesser circulation secondary to parenchymal involvement. Its diagnosis

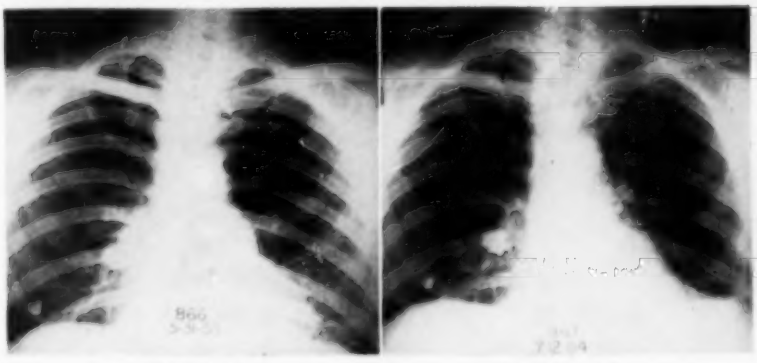


FIGURE 1 FIGURE 2

Figure 1 (Case 1): July 31, 1953, preoperative x-ray.—*Figure 2* (Case 1): July 12, 1954, follow-up one year postoperative.

increases the hazards, but does not necessarily stand as a contraindication, to surgery. The patient's incapacity usually stems from the underlying pulmonary disorder and improvement with surgery can be expected until the circulatory abnormality reaches an advanced stage. Presence of hemoconcentration is important in the emphysema patient for, although cor pulmonale can exist without any alteration in the hematocrit, one should always consider the strong possibility of coexistent cor pulmonale when polycythemia is present to any degree.

Surgical Treatment of Bullous Emphysema

Various surgical measures have been employed for the treatment of emphysematous bullae, ranging from needle aspiration,[11] tube drainage,[1] exteriorization of the cyst area,[12] pulmonary resection,[4] simple excision[12]

FIGURE 3 FIGURE 4

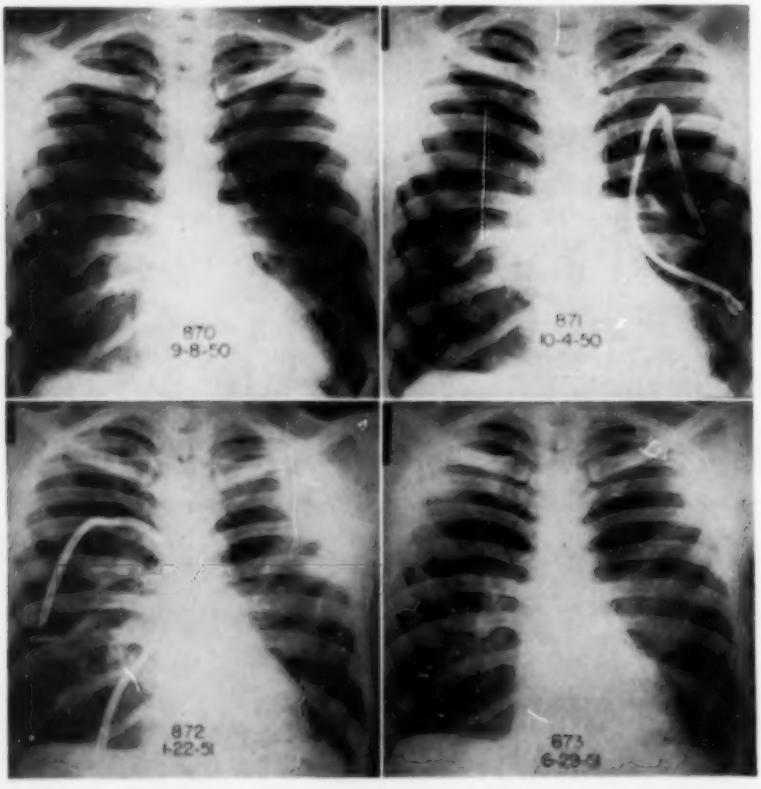


FIGURE 5 FIGURE 6

Figure 3 (Case 2): September 8, 1950. Preoperative film showing large bilateral bullae.—*Figure 4* (Case 2): October 4, 1950. X-ray showing catheter drainage of large bulla, left.—*Figure 5* (Case 2): January 22, 1951. X-ray showing catheter drainage of large bulla, right.—*Figure 6* (Case 2): June 29, 1951. Follow-up x-ray showing ultimate result of bilateral catheter drainage procedure.

and various experimental autonomic denervation procedures[2, 3, 5] used alone or in combination with one of the aforementioned procedures.

Needle aspiration is included only to be condemned as a therapeutic procedure except in instances of sudden acute tension in a large cyst where it may be life saving. Its use in the average case is not desirable since it is not curative and carries a risk of infection, bleeding and secondary tension pneumothorax.

The two-stage catheter suction drainage procedure, as advocated by Head and Avery, has a definite place in the treatment of the severely ill patient with incapacitating bilateral lesions. However, as our experience with the transthoracic approach increases, the field of usefulness of tube drainage progressively narrows.

Exteriorization of the cyst area, which is usually carried out by employing an Eloesser flap, is mentioned only to be condemned. The inevitable infection and prolonged course make this procedure undesirable.

FIGURE 7

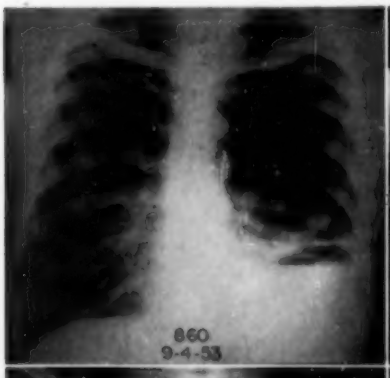
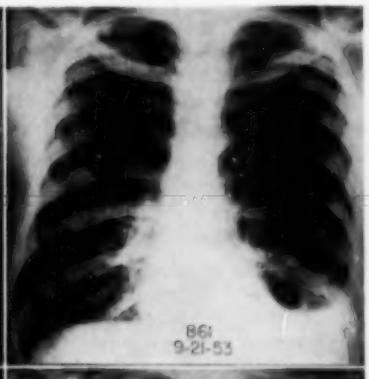


FIGURE 8



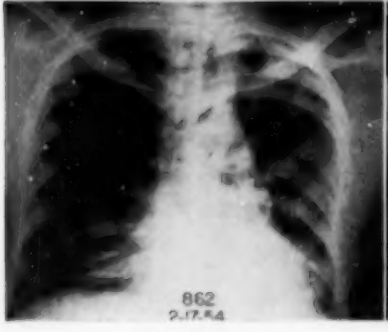


FIGURE 9

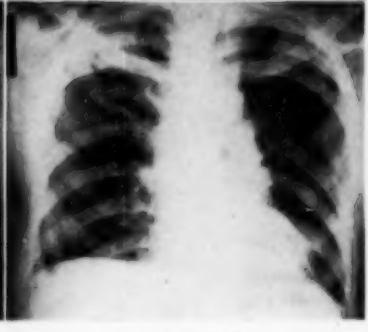


FIGURE 10

Figure 7 (Case 3): September 4, 1953. Initial x-ray showing bilateral bullae and left empyema.—*Figure 8* (Case 3): September 21, 1953. Closed thoracotomy for empyema, left.—*Figure 9* (Case 3): February 17, 1954. Postoperative film following excision of bullae, left.—*Figure 10* (Case 3): March 1, 1954. Film following bilateral excision of bullae.

As to pulmonary resection, in the treatment of bullous emphysema, we would like to interject a word of caution on its use in the average case. Granted, if we are dealing with a Type I patient where only one lobe, segment, or subsegment is involved, or if underlying bronchiectasis is present, pulmonary resection might be indicated. However, these cases are the exception rather than the rule and the average case that the surgeon encounters has Type II bullous emphysema. In these cases, maximum preservation of pulmonary parenchyma is mandatory and formal pulmonary resection is seldom indicated. Maier[13] has stated, and our experience parallels his, that following removal of bullae one frequently is left with a lobe that shows little tendency to reinflate and the unexperienced frequently resect the remainder of the lobe on this indication. He emphasizes the point that this is not an indication for resection and that such a segment will re-expand postoperatively if not removed.

The excision of space-occupying lesions is, in our opinion, the most universally accepted method of treatment of bullous emphysema. We employ an open excision technique approaching the bullae and blebs in the order of their size. The cysts are opened, their boundaries delineated, and excision is carried out down to their encroachment on the underlying parenchyma. The bed of these air-spaces usually consists of parenchyma with numerous bronchial communications. Large bronchial communications are treated by individual suture and all bleeding points can be controlled at this time. If we are dealing with blebs one can usually approximate the adjacent pleural surfaces after the cyst has been excised without leaving deadspace in the parenchyma. If the space-consuming cyst is a true bulla, its bed creates a defect that extends down into the parenchyma that requires a succession of purse-string sutures or mattress sutures for its obliteration. Pleuralization of the area is then accomplished if feasible.

FIGURE 11 FIGURE 12

Figure 11 (Case 4): October 8, 1952. Preoperative film.—*Figure 12* (Case 4): September 29, 1954. Follow-up film, postoperative excision of bullae, right.

A point that frequently arises, where numerous bullae and blebs are encountered, is when to stop excising or how many of the smaller blebs and bullae should be left at the termination of the procedure? The answer to this question lies in the original purpose of the operative procedure, namely, the eradication of space-consuming cysts with a restoration of function to areas of lesser involvement compressed by these cysts. Therefore, if the larger space-consuming bullae and blebs are removed the numerous smaller cystic areas can be left undisturbed without serious consequence. In fact, one most probably achieves a greater degree of functional return by leaving them undisturbed than would be achieved by the numerous suture lines necessitated by their excision.

As to the future development of larger space-consuming cysts from retention of the smaller bullae and blebs, we have never seen progression of these structures in a lung that has had the larger cysts removed. Head[1] has suggested that a free pleural space is necessary for the formation of bullous structures and it is our opinion that the inevitable development of pleural symphysis following thoracotomy prevents the progression of existing bullae or the formation of new bullae and blebs. In support of Head's contention it is interesting to note that of the 17 transthoracic procedures performed in this series, 13 had a free pleural space. Of the four patients that had obliteration of the pleural space three had a history of spontaneous pneumothorax and the other was asthmatic with a history of several bouts of pneumonia. It is safe to assume that bullous emphysema antedated the pleural obliteration in each of these patients.

The use of autonomic denervation procedures in hypertrophic emphysema, with or without bullous formation, evolved from the employing of similar procedures in the treatment of bronchial asthma. In 1952[2] Abbott and his associates reported results on almost every conceivable autonomic nerve operation performed on the emphysema patient and from their vast experience have evolved an operation employing the following: Complete vagal denervation, removal of the upper dorsal sympathetic ganglion chain, severance of the pulmonary ligament and perivascular and peribronchial dissection. They refer to this procedure as "complete pulmonary plexectomy." In addition to this rather complete denervation procedure, existing bullous areas and unilateral foci of emphysema, which they feel

TABLE I

RELATIONSHIP BETWEEN AGE OF PATIENT AND RESULTS OF SURGERY

Age Group	No. of Cases	IMPROVEMENT		
		Marked	Moderate	No Improvement
20 - 30	1	1		
30 - 40	4	3	1	
40 - 50	1	1		
50 - 60	8	4	3	1

represent trigger areas producing reflex bronchial and anteriolar irritability, are excised. A parietal pleurectomy with poudrage is then performed for the purpose of establishing a collateral blood supply from the intercostal vessels through the vascularized adhesions so produced. The procedure of denervation, excision and pleurectomy has also been advocated by Crenshaw[5] who is due the credit for the addition of poudrage.

Any attempt to summarize all of the experimental studies with the various autonomic denervation procedures would be a separate presentation. It can be stated, however, that denervation procedures remain in the realm of experimental surgery and the final chapter in their use is yet to be written. Abbott and his associates have approached the problem in a most scientific manner and admit the failure of this procedure in the so-called "desperation" cases with fixed emphysema in whom little if any useful lung tissue remains. Their best results are obtained in patients with diffuse pulmonary emphysema in whom there is a unilateral focus of emphysema or a trigger area producing reflex bronchial and vascular spasm, the benefits of surgery decreasing as these areas present bilaterally.

Results

Our series consists of 16 cases of bullous emphysema. Thirteen had unilateral operations and three had bilateral surgical procedures. All were treated by local excision of the larger space-occupying bullae except two. One of these received a bilateral catheter drainage procedure and the other had right upper lobectomy performed at another institution with subsequent excision of contralateral bullae after his transfer to our service.

Two of the patients in this series fall into the Type I category with localized emphysematous changes. In each of these cases the bullae were excised and the results of surgical treatment have been excellent. This leaves 14 in the Type II category and it is with this group that the following results will be concerned.

Of the 14 Type II patients, nine (64 per cent) have shown marked improvement and four (29 per cent) have had slight to moderate improvement. Only one (7 per cent) has had no improvement. He had a 20 year history of chronic bronchitis that had early changes of cor pulmonale at

TABLE II

COMPARISON BETWEEN DURATION OF SYMPTOMS AND IMPROVEMENT WITH SURGERY

Duration of Symptoms	No. of Cases	IMPROVEMENT		
		Marked	Moderate	No Improvement
2 years or less	6	3	3	
2 - 5 years	1	1		
5 - 10 years	5	4	1	
10 - 20 years	2	1		1

the time surgery was performed. The operative mortality was 0 per cent and all of the original 16 patients are living at the time of this presentation.

We will now attempt to correlate postoperative improvement with such factors as age, duration of symptoms, time interval since surgery, severity of symptoms and presence of associated conditions. A brief summary will also be included as to the comparative improvement in unilateral and bilateral bullae treated with single or bilateral operative procedures.

In Table I, we have attempted to correlate the age of the patient with the ultimate results of surgery. The fact that the majority of patients fall into the 30-40 and 50-60 year age group is understandable when one considers that these are war veterans who represent World War II and World War I average age groups. The slight disparity between the older age group and those in the younger categories is understandable when one considers that symptom duration and degree of involvement was greater in this decade of observation. The fact that half of our entire series fell into the 50-60 year age category demonstrates that age is not a contraindication to excisional surgery.

The duration of symptoms does not reflect on ultimate improvement as shown in Table II. Our most encouraging results are obtained in patients whose symptoms have persisted over two years. This can be explained by the fact that they have lived with their infirmity for a longer time and are better able to truly evaluate postoperative improvement.

The severity of dyspnea usually parallels the extent of emphysematous involvement and one would expect a marked disparity to exist between those admitted with marked dyspnea and those demonstrating dyspnea in a more moderate degree. However, examination of Table III illustrates that these two groups compare favorably and, from the clinical standpoint, some of our most encouraging results have been obtained in the patient that is almost totally incapacitated, by dyspnea, prior to the operative procedure.

In a progressive disorder such as hypertrophic emphysema one would expect a steady decline in the degree of improvement as the time interval increases from the time of surgery. Examination of Table IV indicates that this supposition is not true and one can frequently predict, with a high degree of accuracy, the long-term results of surgery from the observations made in the early postoperative period.

TABLE III

CORRELATION BETWEEN SEVERITY OR DYSPNEA AND RESULTS OF SURGERY

Severity of Dyspnea	No. of Cases	IMPROVEMENT		
		Marked	Moderate	No Improvement
Marked Dyspnea	10	6	3	1
Slight to Moderate Dyspnea	4	3	1	

With the exception of chronic bronchitis, associated conditions do not alter the degree of improvement to any appreciable extent. Perusal of Table V illustrates that some of the most satisfying results are obtained in the emphysema patient with bronchial asthma. The majority of them have had symptoms for many years and are forever grateful for any degree of symptomatic improvement. By comparing the results obtained in those with emphysema alone and those with an associated bronchial asthma, it is evident that the latter has an equal chance for improvement with the uncomplicated case. The cor pulmonale category emphasizes the fact that this finding in its earlier stages does not necessarily contraindicate surgery. Some degree of subjective improvement may be expected in these patients but the results will not be as enduring as that found in the other categories.

Table VI illustrates the point that, in cases with bilateral bullous formation bilateral operation is always desirable but is not always necessary to obtain a high degree of subjective improvement postoperatively. This is especially true where bilateral operation might jeopardize the life of the patient and in such cases we must accept the results obtained on the side of maximum involvement. In the majority of cases these results are most gratifying.

Case 1: R. M., a white male, 37 years of age, was admitted on June 1, 1953, with a diagnosis of bullous emphysema involving both apical areas of the lungs.

Ten days prior to admission he was awakened from sleep with a severe pain in his right anterior chest, which radiated down his right arm to the fingers. His family physician prescribed codeine and aspirin. He was away from work for the following four days when his pain subsided. On returning to work an x-ray film of the chest revealed large bilateral apical bullae. No previous history of dyspnea could be obtained and he was entirely asymptomatic on admission.

Physical examination revealed a well nourished and developed white male. The thoracic cage was of normal contour and pertinent findings consisted of decreased breath sounds over the apical portions of both lung fields. Hyper-resonance was elicited over these areas but vocal sounds transmitted in a normal fashion. X-ray film examination confirmed the presence of the bilateral apical bullae with marked compression of the subjacent pulmonary parenchyma. A calcified lesion was noted at the right base with calcification of the corresponding draining hilar lymph node.

Angiocardiography and bronchography demonstrated normal vascular and bronchial patterns in both lung fields with displacement of these normal structures by the space-occupying cysts. Preoperative respiratory function studies revealed a maximum breathing capacity of 114.45 L/min. with a total vital capacity of 2900 cc., 65 per cent being contributed by the right lung and 35 per cent by the left on differential study. The total oxygen consumption was 575 cc., 65 per cent being contributed by the left lung and 35 per cent by the right.

Left exploratory thoracotomy was performed on August 3, 1953 under cyclopropane-

TABLE IV

INFLUENCE OF TIME INTERVAL SINCE SURGERY ON SYMPTOMATIC IMPROVEMENT

Time Interval Since Surgery	No. of Cases	IMPROVEMENT		
		Marked	Moderate	No Improvement
6 months to 2 years	6	3	3	
2 years to 5 years	4	4	0	
5 years to 10 years	4	2	1	1

ethylene anesthesia. Two emphysematous blebs were observed arising from the apical-posterior segmental region of the left upper lobe. One of these blebs measured approximately five inches in diameter and the other approximately two inches. No adhesions were encountered. These blebs were excised down to their encroachment on the underlying parenchyma and bronchial communications were secured by individual suture. After control of all bleeding points the area was pleuralized by means of an interlocking suture of 000 chromic cat-gut. No emphysematous changes were present in the remainder of the left upper lobe and the left lower lobe was normal in every detail. The pleural space was drained by means of a No. 30 F colon tube and a No. 30 F dePezzer catheter. A Stedman pump, adjusted to 15 cm. H_2O negative pressure, was attached to the catheters and re-expansion was accomplished within 48 hours. The postoperative course was entirely uneventful.

Postoperative x-ray films show complete re-expansion of the remaining left lung. Respiratory function studies show an increase in the maximum breathing capacity to 152 L/min. The total vital capacity was 3850 cc. with the right side contributing 52 per cent and the left side 48 per cent. The total oxygen consumption was 483 cc., the right side contributing 55 per cent and the left 45 per cent.

This represents Type I bullous emphysema patient who, discounting symptoms of right spontaneous pneumothorax, was asymptomatic both before and after surgery. Respiratory function studies reveal marked improvement in the function of the left lung following the excisional surgery. He has returned to work and will be admitted at a subsequent date for contralateral operation.

Case 2: R. R., a colored male, 32 years old, was admitted on September 8, 1950, with a diagnosis of bilateral bullous emphysema and bronchial asthma.

The present condition had its onset in 1943 with an attack of bronchial asthma. During the ensuing five years the asthmatic attacks became more frequent and severe. In 1948 emphysematous changes were first noted and by the spring of 1950 large air-cysts were demonstrable in both lung fields. Marked dyspnea on the slightest exertion had been a prominent symptom for the past two years and a state of almost complete incapacitation had been reached by the time of his admission.

Admission roentgenograms revealed marked bilateral hypertrophic pulmonary emphysema with large apical bullae occupying approximately two-thirds of the left pleural space and approximately one-half of the right. Angiocardiography was not performed and bronchography and respiratory studies were omitted because of his poor general condition.

On September 8, 1950, pleural fusion was accomplished on the left by removal of the anterior segment of the 2nd rib and the insertion of an oxycel sponge on the parietal pleura. On October 2, 1950, a No. 22 fenestrated catheter was inserted into the left apical bleb. The air-cyst obliterated in one month at the end of which time the catheter was removed. On December 15, 1950, pleural fusion was performed on the contralateral side with insertion of a fenestrated catheter on January 10, 1951. This bleb was obliterated within three weeks and the catheter was removed.

Improvement during the postoperative period was marked and he was restored to restricted, but useful, life in so far as dyspnea was concerned. He was placed in the moderate improvement category of the accompanying tables. Improvement has persisted during the past four years.

TABLE V

THE EFFECT OF RELATED CONDITIONS ON ULTIMATE IMPROVEMENT

Related Condition	No. of Cases	IMPROVEMENT		
		Marked	Moderate	No Improvement
Emphysema Alone	7	5	2	
Emphysema with Chronic Bronchitis and Early Cor Pulmonale	1			1
Emphysema and Bronchial Asthma	5	4	1	
Emphysema and Early Cor Pulmonale	1		1	

Case 3: O. S., a colored male, 34 years old, was admitted on September 4, 1953, with a diagnosis of bilateral bullous emphysema complicated by left spontaneous pneumothorax, with subsequent empyema formation. On admission he was toxic and had a fever of 104° F.

He gave a history of progressive dyspnea for the previous eight months. In June 1953, he developed sudden pain in the left chest. His family physician administered two injections of penicillin. Following this his condition progressively deteriorated and by August he had developed productive cough accompanied by streaking. The expectorated material became purulent and he was admitted to the Veterans Administration hospital, Fayetteville, N. C. where the aforementioned diagnosis was established.

On admission closed thoracotomy, left, was performed with marked improvement in his general condition. The empyema pocket obliterated within two weeks and the catheter was removed. Angiocardiography and bronchography were not performed. Respiratory function studies showed a maximum breathing capacity of 57.2 L/min. Total vital capacity was 3040 cc. with the right lung contributing 93 per cent and the left lung 7 per cent. The total oxygen consumption was 387 cc./min. with the right side contributing 90 per cent and the left side 10 per cent.

Left thoracotomy was performed on October 23, 1953, under cyclopropane-ethylene anesthesia. Pleural symphysis was complete. Two large blebs and numerous smaller bullae were removed from the left upper lobe. Several blebs and bullae were removed from the left lower lobe. Hypertrophic emphysematous changes were marked throughout the remaining pulmonary parenchyma. The pleural space was drained by a No. 30 F colon tube and dePezzer catheter attached to —15 cm. of H_2O negative pressure. Re-expansion was complete within 72 hours and the tubes were removed. His postoperative course was uneventful and improvement was marked.

Postoperative respiratory physiological studies revealed a total vital capacity of 2350 cc. with the right side contributing 77 per cent and the left 23 per cent. The total oxygen consumption was 300 cc./min., the right side contributing 67 per cent and the left 33 per cent. A maximum breathing capacity determination was not performed at this time.

On February 18, 1954, right thoracotomy was performed. The pleural space was free of adhesions. Three large space-occupying bullae were present in the right upper lobe and one large air-cyst was excised from the lateral basal segment of the right lower lobe. Five other moderately sized bullae and blebs were excised from the remaining portions of the lung. The pleural space was drained and negative pressure applied for the first 48 hours when complete re-expansion had occurred. His postoperative course was entirely uneventful.

This is Type II bullous emphysema with bilateral bullous involvement. He was treated with bilateral excisional surgery and marked improvement was obtained.

He was readmitted on July 9, 1954 for bronchospirometric study and evaluation. On this admission his maximum breathing capacity was 48 L/min. Total vital capacity was 2675 cc., the right side contributing 69 per cent and the left 31 per cent. The total oxygen consumption was 325 cc./min., the left lung contributing 39 per cent and the right 61 per cent.

TABLE VI

COMPARATIVE RESULTS ON PATIENTS WITH UNILATERAL AND BILATERAL BULLAE RECEIVING A UNILATERAL OR BILATERAL OPERATIVE PROCEDURE

	No. of Cases	IMPROVEMENT		
		Marked	Moderate	No Improvement
Bilateral Bullae with Unilateral Excision	6	3	2	1
Unilateral Bullae with Unilateral Excision	5	3	2	
Bilateral Bullae with Bilateral Excision	1	1		
Bilateral Bullae with Unilateral Lobectomy and Thoracoplasty and Contralateral Excision	1	1		
Bilateral Bullae with Bilateral Head Procedure	1	1		

Case 4: F. K., a white male, 48 years of age, was admitted in September 1952, with a diagnosis of bilateral bullous emphysema and bronchial asthma.

The present condition had its onset in 1944 with an attack of bronchial asthma. During the ensuing five years the asthmatic attacks became more frequent and severe and in 1949 he noticed progressive dyspnea during stages of remission from asthmatic attacks. Roentgenograms taken at that time revealed bilateral hypertrophic emphysematous changes with bilateral bullous formation. During the next three years dyspnea became progressively worse and by the time of admission he was almost totally incapacitated.

At the time of admission x-ray films revealed marked bilateral bullous emphysema. Angiocardiographic and bronchographic examinations were not performed. Respiratory function studies demonstrated a maximum breathing capacity of 33.6 L/min., with a total vital capacity of 3100 cc., 54 per cent being contributed by the right lung and 46 per cent by the left. The total oxygen consumption was 266 cc./min., the right lung contributing 25 per cent and the left lung 75 per cent.

Right thoracotomy was performed on October 16, 1952. The pleural space was found to be free of adhesions. Two large blebs, each occupying approximately one-fifth of the pleural space, were removed from the right upper lobe. Several smaller bullae and blebs were removed from the upper and lower lobes. Drainage of the pleural space was accomplished by means of a colon tube and a deFezzer catheter attached to —15 cm. H_2O negative pressure. Re-expansion was complete in 72 hours but the tubes were left in situ for five days because of a small but persistent air leak.

Postoperative improvement was marked and, although his activities are restricted, he has returned to a useful life and a gainful occupation. This is a Type II bullous emphysema with unilateral excision performed. His general condition is such that contralateral surgery is not indicated.

He was readmitted for further observation on July 9, 1954. A maximum breathing capacity determination performed at that time showed 57.0 L/min. His total vital capacity was 2025 cc., the right lung contributing 56 per cent and the left 44 per cent. The total oxygen consumption was increased to 505 cc./min., the right lung contributing 32 per cent and the left lung 68 per cent.

CONCLUSIONS

Over-all results of excisional surgery for emphysematous bullae and blebs are most gratifying and the fact that 93 per cent of this small series obtained some degree of improvement following operation makes this method of surgical management compare favorably with other forms of treatment found in the present day literature. If the fact that we are striving for an improvement of symptoms, rather than a cure, is constantly kept in mind, many patients with severe degrees of pulmonary incapacitation can be restored from a state of marked infirmity to a restricted, but useful, life.

CONCLUSIONES

Los resultados globales de la cirugía excisional de las bulas y ampollas enfisematosas son muy satisfactorios y el hecho de que 93 por ciento de esta pequeña serie obtuvieron algún grado de mejoría después de la operación, hace que este método se compare favorablemente con otras formas de tratamiento encontrados en la literatura actual. Puesto que se trata de mejorar los síntomas más que de obtener una curación y esto se conserva en la mente, muchos enfermos con grados severos de incapacidad respiratoria, pueden restaurarse de un estado de marcada incapacidad a una vida con restricciones pero útil.

RESUME

Les résultats exceptionnels de la chirurgie d'exérèse pour les bulles et vésicules emphysémateuses sont des plus satisfaisants. Le fait que 93% des malades de ce petit groupe obtint quelque degré d'amélioration après

l'opération permet de comparer favorablement cette méthode d'intervention chirurgicale aux autres modalités de traitement, signalées dans la littérature actuelle. Si le fait que nous nous efforçons d'améliorer les symptômes, plutôt que de les guérir, est constamment présent à l'esprit, beaucoup de malades atteints à un degré sérieux de déficit pulmonaire peuvent être améliorés et passer du stade d'une grave infirmité à une vie diminuée, mais utile.

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Angiocardiography: Its Development, Technic, and Findings, and Role in Surgical Heart Disease*

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The development of surgical procedures to correct or ameliorate certain cardiovascular anomalies has created a need for precise diagnosis and exact delineation of the defects present. To satisfy this need, all of the diagnostic tools at our command, including the newer methods, such as catheterization and angiocardiography, are employed. The angiocardiographic method aids in the recognition of the defect and may occasionally supply precise delineation of the exact abnormality present. It has thus contributed immeasurably to the understanding of the pathologic physiology involved. It is not a substitute for the older, simpler and more basic diagnostic approaches, but rather supplements them.

My colleagues on this panel will discuss the diagnostic problems in this field and I will confine myself to a general discussion of the role of angiocardiography in these problems, with specific examples of the findings in certain types of anomalies, and a review of the development of the method and technic.

Angiocardiography or cardio-pulmonary angiography is the roentgen study of the internal structures of the heart and great vessels, and of the vessels of the lesser circulation, by means of a radio-opaque medium injected into the circulation, usually intravenously.

The first satisfactory studies were made in 1931 by Moniz, Carvalho and Lima[1], using catheters, and by Castellanos[2] using direct injection into the antecubital vein. The agent used in both instances was concentrated sodium iodide solution, which produced severe reactions, and after a few attempts, this approach was abandoned. As suitable organic iodine compounds became available, Castellanos and his co-workers devised an intravenous technic for angiocardiography, also coining the term. Robb and Steinberg[3,4] after a great deal of fundamental physiological and clinical investigation, evolved the present technic.[5] This method consists of the rapid intravenous injection of approximately 50 cc. of an appropriate contrast agent, using a large bore needle and syringe, and making a suitable number of films of the heart, great vessels and lungs during the course of their opacifications.

In the past decade and a half, this method has been modified and perfected to permit its use as a diagnostic procedure which is almost routine. This has been a significant achievement, yielding much fundamental information about the anatomy of the heart, lungs and mediastinum, and alter-

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ing many old concepts about these structures. There are, however, limitations to the method. It is not without danger to the patient, and in many instances adds little to what is already known. These points will be discussed later.

Technic

Of primary importance in the technic is the injection equipment. It is absolutely necessary to use a large bore needle and syringe, so that the injection may be achieved in less than two seconds. The Robb modification of the Lindeman needle (12 gauge) is preferred. The patient is prepared by omitting the meal before the examination, and may be given a barbiturate such as seconal (100 mgm.). Small children and uncooperative adult patients should be anesthetized. After the needle is inserted, patency is checked by observing the ease of injection of a small quantity of saline solution. A circulation time determination is made, if this has not already been done, and then the patient is positioned at the x-ray apparatus, injection of the contrast agent is carried out, and the exposures made. The number and intervals of exposures depend on the equipment available. The exposures should be short — 1/20th second or less — necessitating x-ray equipment of 300 milliamperes or more. Since the times of opacification of the various structures depend on the circulation time, the times of the exposures should be adjusted accordingly, if the circulation times are normal. In the normal, the times of opacification are:[5]

	(Time after beginning of injection)
Superior vena cava	0.5 - 1.5 seconds
RA	1 - 2
RV	1.5 - 2.5
PA	2.0 - 3.5
Pulmonary veins	5 - 7
LA	5 - 8
LV	7 - 10
Thoracic Aorta	7 - 10

The difficulty in determining the time of a single exposure or two exposures, and the frequent failure of such procedures have stimulated the development of many devices, simple and complex.

The use of an automatic rapid film changer[6] practically eliminates any chance of error due to timing and achieves a more complete visualization of the dynamic changes in the heart and great vessels. There are two popular devices available, the Sanchez-Perez serial cassette changer, a considerable refinement of the push-box idea. This uses 12 special cassettes and is capable of 0.5 second exposures. There is also available the Fairchild roll film cassette, also capable of 0.5 second exposures. The latter has been widely used and also incorporated into several special devices such as the Chamberlain biplane stereoscopic unit which makes stereoscopic films in both planes with a single injection. Other devices use the principle of a motion picture camera with a lens of large aperture photographing a fluoroscopic screen. While this type of device can produce

exposures in rapid sequence, the amount of radiation which the patient receives is unfortunately quite large. A method which holds considerable promise is the use of image amplifying electronic tubes in conjunction with the fluoroscopic screen and the motion picture camera set-up just mentioned. While this is still in the experimental stage, the results thus far have been encouraging. The dose of radiation is no greater than that received during ordinary fluoroscopy. Other devices, particularly the Elema and Schonander, are capable of exposures at rates up to 12 per second. This is perhaps an optimum rate for general use.

At the present time, the agent of choice is Urokon (70 per cent). We have encountered no report of death due to its use in angiocardiography. Nevertheless, its use should be approached carefully, especially in cyanotic or debilitated individuals. Concentrated diodrast and neo-iopax have been used for many years. Approximately 35 deaths[7,8] have been reported in angiocardiographic studies in which these agents were employed, principally in cyanotic children and usually after the second or third injection. Of course, a sensitivity test should be performed in every instance, and if a reaction occurs, the angiocardiogram should be abandoned.

The subjective reaction to the contrast agents[5] consists of a bitter taste in the patient's mouth occurring about 10 seconds after injection, followed by a sensation of intense heat sweeping the entire body, but passing quickly, and a feeling of extreme weakness and dizziness. Occasionally, nausea and vomiting occur. Upon occasion, shock and syncope, respiratory arrest, and, rarely, death may occur in a few minutes. In a few cases, there is arm pain. Cough may occur during the period of pulmonary filling. Urticaria is observed in 5 to 10 per cent of cases where diodrast is used, but rarely with urokon.

Objectively, there is often an initial bradycardia, always followed by a moderately prolonged and rather marked tachycardia. The blood pressure falls precipitously, then rises slowly. Occasionally, there are arrhythmias and frequently electrocardiographic tracings reveal transient changes in the QT segment and T-wave depressions, suggesting myocardial ischemia. These changes have been one of the reasons that investigators have been loath to study the coronary arteries in man with contrast agents. In approximately 80 to 90 per cent of cases, there is local thrombosis of the vein of varying degree. No emboli have been reported.

The dose of the contrast agent is approximately 50 cc. in adults with normal sized hearts. In greatly enlarged hearts, 75 cc. or more may be used, with the larger 100 cc. syringe. In children, roughly 1 cc. per kgm. is the quantity used. With high speed, high capacity x-ray equipment, a smaller dose is often possible at all ages.

The position of choice for the patient varies with the diagnosis or condition being studied and should be checked by a control or test film made before injection. In general, oblique positions yield more information than straight PA or lateral views, again depending on the condition. The obliques should be extreme, and be of the order of 60° to 70°. Preliminary fluoroscopic study is of great value in determining the optimum view. With

biplane devices, this problem is minimized to a considerable degree.

A modification of the above technic utilizes injection of contrast agent through a large bore catheter introduced into the superior vena cava or into the chamber being studied. The procedure may be performed as a combined operation with conventional cardiac catheterization.

Direct aortography, either by direct puncture or catheterization from above or below, has been developed so as to supply more information concerning the aorta and its branches, and achieves, when successful, superior visualization of aortic abnormalities, patent ductus, and so forth. It offers a potentially better evaluation of the left heart and has incidentally succeeded in visualizing the coronary arteries in a number of instances. A complete discussion of this procedure is somewhat beyond the scope of this paper, although it should be noted that it carries a considerably greater risk.

General Indications

Cardio-pulmonary angiography should be performed only after a complete cardiac or pulmonary work-up has been carried out, although it may be done before cardiac catheterization. It should follow, from the roentgen standpoint, careful fluoroscopy, roentgenography, and possibly planigraphy. It has perhaps its greatest value in congenital heart lesions in children,[6] and is indicated in certain cases in which surgery is contemplated, so that the nature and location of abnormalities can be elucidated, and in all cases where the diagnosis is uncertain and where surgery might help if an operable lesion could be found. The value of the procedure in acquired heart disease is, in general, considerably less, and it probably should not be part of the usual work-up. It is indicated, however, in many cases where surgical intervention is being considered, and again, in selected cases where the diagnosis is obscure. Angiographic studies of hearts with mitral lesions[5] have frequently been of value in determining the degrees of insufficiency present, and in fact have occasionally revealed an unsuspected degree of insufficiency. Since a significant degree of insufficiency is considered at the present time to be probably a contra-indication to valvulotomy,[9, 10] such knowledge may obviate a dangerous and probably unnecessary procedure.

Angiocardiography is of value in leutic heart disease with or without obvious aortitis, since early widening of the aorta is detected with considerable frequency. Obvious aneurysm, any mass in which the diagnosis of aneurysm is considered, and dissecting aneurysm are also indications for the procedure. Other indications include mediastinal tumors in which surgery is being considered or which cannot be diagnosed by ordinary means. Also, it is useful in problems involving pericardial effusion and peri-carditis, as well as certain pulmonary lesions, such as selected cases of bullous emphysema, arteriovenous fistula and certain inflammatory processes where the knowledge of status of the circulation is important. The study of pulmonary vascular structures is currently in progress at many centers and the knowledge being gained, while much less spectacular than the demonstration of a coaretation, for example, will probably be

of great importance in what it will teach us to see in ordinary films, and in our understanding of the diseases themselves. For example, we have gained new concepts of the appearance of the lung markings in pulmonary hypertension from such studies.[11]

Obviously, angiocardiography is not usually indicated in heart and lung problems where it has consistently failed to be of value. For example, it is of little use to study a simple interventricular or interatrial shunt in adults with ordinary technic and equipment[12] and an angiogram of an atherosclerotic aorta tells us little that we ordinarily do not already know. Angiocardiography probably should not be performed in very ill individuals, or in patients with severe asthma or allergies, or those who are sensitive to the contrast agent.

Normal Findings

The findings are composite ones based on correlation of a large number of normal studies[5] with conventional chest films and with anatomical and autopsy material. In the PA projection, the right heart border is composed of the right innominate vein, superior vena cava, and the lateral aspect of the right atrium. In older individuals, the aorta may be border forming in the right upper margin. The largest portion of the diaphragmatic border is right ventricle. The left border consists of, from above down, the aortic arch (knob), pulmonary artery, the left auricular appendage, and left ventricle. The left atrium and pulmonary conus (infundibulum) are not border-forming on the left, in the normal.

In the left anterior oblique, the aorta forms the bulge of the cardiac silhouette anteriorly. The aorta, it should be noted, originates somewhat more posteriorly. The main pulmonary artery and occasionally the pulmonary conus form the curve below this, and the right auricular appendage projects anteriorly. This is occasionally seen on conventional films. Often the right atrium forms the extreme anterior limit with the right ventricle slightly posterior and superimposed. Occasionally the right ventricle forms the anterior border, especially in marked obliquity and in ventricular systole. The diaphragmatic margin is anterior to the superimposed right atrium, right ventricle and left ventricle, with left ventricle forming most of the diaphragmatic and posterior border, except superiorly where the left atrium is seen, with its associated pulmonary veins.

In lateral projection, the structures forming the borders are quite like those of the left anterior oblique view. However, the right atrium does not form the anterior border, but pulmonary artery, pulmonary conus and right ventricle form the anterior margin of the heart.

The right anterior oblique view reveals the superior margin of the anterior border is formed by the curve of the ascending aorta. Below another curve is formed by the pulmonary artery (and conus rarely), merging with the anterior portion of the left ventricle, which extends to the diaphragm. Posteriorly is the left atrium above, and right atrium below, with the RV forming most of the diaphragmatic surface.

After the injection, the arm veins, the basilic and cephalic, will be seen, then the axillary, sub-clavian and innominate veins. The innominates join

to fill the superior vena cava, which is seen approximately 1 to 1½ seconds following injection. The size of the vena cava varies widely, from 7 to 20 mm.in PA, the average being 13 mm. The right atrium then fills, and occasionally there is reflux into the inferior vena cava and hepatic veins. The right atrium is an oval, thin-walled structure best seen in the PA and left anterior oblique views. The right auricular appendage projects anteriorly and medially. There are considerable variations in size and shape in the normal. In the left anterior oblique projection, the left atrium lies posteriorly and mixing or shunt is best seen in this view. The right ventricle has a generally conical appearance, with the base on the diaphragm and the apex pointing into the pulmonary valves. The outflow tract is anterior but is not border-forming on the left. It consists of conus or infundibulum and valve area. The tricuspid area through which right atrium blood flows is on the right and the irregular I.V. septum on the left.

The pulmonary artery extends from pulmonary conus for a short distance, passing medially and posteriorly below aortic arch, where it divides normally in right and left branches. It is short and broad, and the valve bulges are seen at origin. The left branch turns sharply inferiorly and branches into superior and inferior branches. The various branches of each pulmonary artery have been accurately mapped in great detail.[5] The size of the major and minor branches varies somewhat from person to person, but a mean range has been established and these values are of use in evaluating pulmonary artery dilatation.[5,12]

The values are:

Area	*Range*	*Average*
A) Conus	16 - 24 mm.	19.1 mm.
B) Main	20 - 30 mm.	26.4 mm.
C) Right branch	17 - 30 mm.	23.4 mm.

The latter measurement is the one commonly used, and can occasionally be gotten from conventional films, although this method is open to question.

The blood return from the lungs through the pulmonary veins is much less easy to see, due to persistence of the contrast agent in the pulmonary arteries. The pulmonary veins are large thin-walled structures, usually two on each side, occasionally three on the right, and occasionally they unite to enter the left atrium as one trunk. They normally enter the left atrium in fanlike fashion, carrying oxygenated blood from the lungs. The left atrium is posteriorly and centrally located and is roughly ovoid or lemon shaped. It is smaller than the right atrium. In the PA projection, it is not border forming, although the auricular appendage may form part of the L-border. In the right anterior oblique, it is seen to lie posteriorly and superiorly.

The left ventricle is now reached through the mitral valve and it is seen that this structure forms the apex of the heart. It is to the left of and behind the right ventricle. In the PA view, the left ventricle presents as an elliptical mass, forming the left border of the heart and reaching the apex. It must be remembered that much of the left ventricle is pos-

terior. The upper portion of the ventricle and the aortic valve area are best seen in the left anterior oblique. The mitral valve region is seen at best with difficulty because of its proximity to the aortic valve. The aorta is best seen in the left anterior oblique projection again. The arch is well visualized and the brachiocephalic vessels can be delineated in many cases. The arch is subject to a great many variations in size and configuration but has a smoothly tapering outline without bulges or narrowing. The size has been evaluated and figures have been published. In general, the length and caliber increase gradually with increasing age. The figures are as follows:[5]

Area	*Range*	*Average*
Ascending aorta	16 - 39 mm.	28.6 mm.
Transverse aorta	13 - 34 mm.	24.8 mm.
Descending aorta	12 - 32 mm.	22.9 mm.

The heart valves vary in visibility. The aortic and pulmonary valves are seen with considerable regularity. The mitral and tricuspid valves are rarely seen and one should refrain from attempting to demonstrate these areas except with high speed serial technics.

Abnormal Findings

Congenital Heart Disease:

The discussion will be limited to the more common and surgically important lesions.

Cyanotic Type: Tetralogy of Fallot and pseudo-truncus arteriosus

Cooley[13] has grouped these two together because of the similarity of the problem, both in the approach to diagnosis and in the surgical procedure involved. Pseudo-truncus arteriosus is his term and is a good one. The surgical procedures[14] in this type of problem depend on certain criteria, which include:

1) The presence of a pressure gradient between the systemic circulation and pulmonic circulation, allowing blood to flow into the pulmonary artery;
2) The presence of vessels of adequate size for the anastamoses;
3) A left to right shunt of un-oxygenated blood.

Angiography can help by determining—

1) The size and position of the aorta, and whether it is on the right or left, if this cannot be precisely determined at preliminary fluoroscopy;
2) The size and status of the pulmonary conus; this is occasionally often untrustworthy even in angiography, but with modern equipment we can usually rule out pulmonic stenosis by this method. Some difficulty exists from the angiographic standpoint in the differentiation of the tetralogy of Fallot or pseudo-truncus, the Eisenmenger complex, or pulmonary stenosis with a closed I.V. septum and reversed inter-atrial shunt;[13, 15]
3) The status of the pulmonary circulation can be determined by angiocardiography. This is also a difficult part of the study to evaluate.

Pcor pulmonary filling may be due to a large amount of blood being shunted into the aorta without significant stenosis being present in the pulmonary artery or infundibulum. The persistence of contrast agent in the right ventricle may give a clue to the presence of stenosis. However, dense early left ventricular opacification is believed to favor pulmonic stenosis with an intact septum and inter-atrial shunt rather than a tetralogy;

4) An interventricular septal defect may sometimes be demonstrated.

In summary then, in tetralogy and pseudo-truncus arteriosus, the aorta is visualized synchronously with the pulmonary artery, or alone without the pulmonary artery being visualized. Occasionally, early filling of the aorta is not visualized, although opacification of some of the branches of the aorta should be sought. The status of pulmonary stenosis may be difficult to evaluate, as is the status of the pulmonary circulation. This is minimized with good films. The interventricular septal defect may occasionally be visualized, particularly in children. It must be admitted that the angiocardiogram, of itself, is occasionally diagnostic in tetralogy of Fallot or pseudo-truncus, and the report rendered is that the appearance is compatible with the clinical diagnosis. Nevertheless, the angiocardiographic investigation is of great value in differentiating this malformation from others, and (with cardiac catheterization) elucidating at least a part of the pathologic changes present prior to surgery.

Tricuspid stenosis:[16,17]

In this anomaly, the defect may vary from a simple narrowing of the tricuspid orifice to a complete absence of the valve, with only a nodule on the floor of the right atrium representing its site. It is always accompanied by a poorly functioning or non-functioning right ventricle. If significant obstruction to the flow of blood from the right atrium is present, a shunt must exist in order to allow blood flow through the lungs and permit survival. This blood flow must be through an inter-atrial septal defect. The return flow to the right ventricle or from the lungs into the systemic circulation may be through:

1) a patent ductus arteriosus;
2) through an interventricular septal defect into the right ventricle and then to the lungs, or
3) through a transposed pulmonary artery from the left ventricle.

Improvement of the condition by surgery depends, to a large extent, on whether the size of the inter-atrial septal defect present is adequate, and if an artificial ductus arteriosus will aid. Angiocardiography will often give detailed knowledge of the pathological anatomy present, as follows:

1) The size of the defect can be evaluated. If it is small, enlarging it will sometimes be of more value than a ductus;
2) If there is an associated transposition of the great vessels, there will be no benefit from a ductus arteriosus;
3) If pulmonic stenosis is present, and it often is, a knowledge of the size and position of the arteries will be helpful. From a practical

standpoint, the angiocardiographic findings in a well developed tricuspid atresia or stenosis are quite diagnostic and reveal a large shunt of blood from right atrium into left atrium. Also, from the practical standpoint, it is not possible to state that the right ventricle is non-functioning, but only that there is non-visualization. A poorly functioning right ventricle is also somewhat difficult to evaluate. However, a transposition of the great vessels, or a dextroposed aorta over-riding the interventricular septum and, less frequently, pulmonic stenosis can be demonstrated.

Transposition of the great vessels:[18]

Most individuals with this disease die in infancy, but it has been observed that those with an interventricular septal defect may survive for a variable period, and if patent ductus arteriosus is also present, even longer survival can be expected. The most common shunt, however, is inter-atrial. The diagnosis of this malformation can be made in most instances without angiography. The characteristic narrow vascular pedicle which becomes large in the left oblique, as described by Taussig,[19] is readily recognized. However, since the surgical approach depends in part on whether inter-atrial septal defect is present, angiocardiography may be employed in order to evaluate the status and nature of shunts and also give data on the pulmonary arteries.

There are, of course, numerous other lesions of the cyanotic variety observed, although these are considerably rarer than those noted above. Angiocardiography may profitably be employed in the study of these lesions.

Acyanotic type:

There is obviously a considerable overlap between the acyanotic and the cyanotic lesions. Eisenmenger's complex, pulmonic stenosis, the various septal defects, and so forth, may in some instances be associated with cyanosis, and in others may show no cyanosis (or belatedly show cyanosis), depending upon the nature and degree of the associated anomalies present. The difference in classification, however, is more than academic since non-cyanotic lesions are usually compatible with survival into childhood and often into adulthood, whereas cyanotic lesions are usually associated with a shorter survival.[5] Again, the nature and location of the defects are frequently well demonstrated by angiocardiography. In most instances, it is possible to make a rather definite diagnosis without contrast visualization.

Coarctation of the aorta:

There is usually little difficulty in establishing the diagnosis by clinical means, assuming that it is considered.[12] Occasionally in an atypical case, there may be a question which can be answered by contrast visualization. The principal value of angiocardiography in this disease is elucidating the site and demonstrating the degree of narrowing before surgery.[22] Occasionally, associated unsuspected lesions are revealed. The method is limited by the technic since, in general, the left side of the heart and the aorta tend to be less well visualized than the right side, and for this

reason, retrograde aortic studies are sometimes employed for this purpose.[23] However, with good technic, the intravenous angiocardiographic technic will produce films of diagnostic quality. Other anomalies of the aorta may also be studied by angiocardiography, but here too it may be desirable to consider the use of direct aortography in some instances.

Inter-atrial septal defect:

The presence of this defect is usually difficult to establish by angiocardiography alone. It has been seen with certainty in children[24, 25] with a reasonable degree of frequency. However, in adults one usually sees only persistent opacification of the right atrium, occasionally re-opacification. This is a finding which should be interpreted with considerable caution, since various technical and non-pathologic cardiac factors may produce it. Indeed, Jonsson[23] states that we should not perform contrast studies in adults where such a diagnosis is fairly certain. Catheterization is better suited to making this diagnosis. With high speed serial technics, however, it may be possible to visualize the defect, even in adults. When tricuspid stenosis is also present, it is more easily visualized.

Inter-ventricular septal defect:

The approach to the study and evaluation of inter-ventricular septal defects should be similar to that of inter-atrial septal defect. I refer, of course, to the simple defects which are presumed not associated with other anomalies. In general, catheterization yields more information.

Patent ductus arteriosus:

This diagnosis can still best be made with the stethoscope. Preoperatively, however, angiocardiography can give valuable information concerning the status of the great vessels, the presence of additional shunts and, occasionally, the size and function of the ductus itself.[5,26] Angiography should never be undertaken, however, with conventional equipment in order to achieve visualization of the ductus. For this purpose, aortography is better suited.[23] With high speed serial technics, it is possible to visualize rhythmic decreases in opacification in the pulmonary artery ("blanding") in many cases of patent ductus arteriosus.

Angiocardiography may demonstrate primary pulmonic stenosis, primary pulmonary artery dilatation and other related abnormalities. The rigorous exclusion of related or additional lesions must be left to other modalities such as catheterization or even autopsy.

There is, however, another non-cyanotic lesion which is subject to angiocardiographic study. This is anomalous pulmonary venous drainage.[5] This disease may simulate an inter-atrial septal defect, which may indeed be an accompanying defect and is readily delineated by angiocardiography. This method has also taught us to suspect this lesion where there are abnormal vascular structures in the central lung fields.

Acquired Heart Disease

Angiocardiographic study is infrequently required in the diseases in this group. However, it has been of considerable value in investigational work, but has not demonstrated that it has a place in the usual workup, except in

certain instances. For example, in the study of arteriosclerotic heart disease, angiocardiography is rarely indicated. Visualization of the elongated aorta in this disease has been of interest, but has little practical value unless simple or dissecting aneurysm is suspected because of symptoms. The sub-acute or chronic variety of dissecting aneurysm lends itself to this type of investigation and the findings have been well established.[5] A characteristic double shadow may be seen, or there may be only irregular narrowing of the lumen. Aortography in this instance is contra-indicated. Ventricular aneurysm and related changes can be demonstrated consistently, and the contrast study is used to complement electrocardiographic and conventional film findings, and cardiac catheterization.[5]

Syphilitic Heart Disease

This is an important indication for contrast study,[5, 27] Small but significant alterations in the contour of the ascending and transverse portion of the aorta may be found. These alterations are slight to moderate widening, irregularity, and occasionally local dilatation. Variations in this thickness of the wall may also be seen. If aneurysm is present, it is usually readily filled if there is not obstructing clot present. Occasionally the sac itself may be filled with clot and visualization not be achieved. Also, a large aneurysm may show only a partial or faint opacification and it is important to use an adequate quantity of contrast solution and to produce films of good quality. Most lesions will opacify and they may be differentiated from non-vascular masses in the mediastinum and lungs.[28] Innominate artery aneurysms are similarly well studied.

Rheumatic Heart Disease

Enlargement of the left atrium is regularly demonstrated in mitral disease. We have learned that the right ventricle is often not much enlarged, although there is usually some hypertrophy of the wall. We have also learned that the pulmonary veins are dilated and may participate in the cardiac deformity seen on conventional films.[5]

In advanced mitral stenosis, there is also demonstrated remarkable stasis in the left atrium with prolonged and pronounced opacification. The left ventricle fills poorly, never becoming as dense as the atrium. The large pulmonary artery in severe mitral stenosis can be opacified and we have learned that the density seen in the conventional films is this structure and not the pulmonary conus. Angiocardiography may aid in establishing the degree or presence of mitral regurgitation, a consideration of importance in evaluating patients for valvulotomy.[10] Vascular changes in the vessels of the lung have been studied and are thought to be of diagnostic importance.[11] Demonstration of "giant" left atrium usually indicates regurgitation.

Pulmonary Heart Disease

The principal value of angiocardiography is in the demonstration of pulmonary artery dilatation. This may be noted centrally with marked diminution of vascular structures in the periphery of the lungs. The sizes of the normal vessel have been reported and enlargement can be determined in most instances. The right ventricle may also be enlarged, but this is

inconstant.[27] It is possible that in a case with known pulmonary heart disease, the pulmonary arteries and left ventricle may be within the normal limits of size. It is probable that these were at the lower limits of normal before the onset of disease, and although remarkable increase has occurred, the vessels were still not above normal limits. Angiocardiography is certainly not indicated in the routine workup in this disease, but may have a value in exceptional cases in excluding other lesions and will serve adequately to visualize the structures in question.

Peri-Cardial Effusion and Constrictive Pericarditis

Angiocardiography may be of considerable value in establishing the diagnosis of peri-cardial effusion or peri-cardial thickening,[30,31] and it has been used for this purpose in a great many instances. Its primary value is probably in its ability to reveal any associated lesions and to de-limit the actual heart size with a great deal of precision. It has been used in our institution to exclude pericardial effusion or thickening in certain instances where other findings suggested that it was present.

SUMMARY

Angiocardiography, a method of contrast visualization of the heart, lungs and great vessel, has its greatest value in the diagnosis of congenital heart anomalies. It is helpful in the delineation of the defects present, and with cardiac catheterization, supplements the conventional methods of examination. It is applicable to a considerable number of the problems seen in practice, and to most of the cases coming to surgical correction. It has contributed greatly to understanding of these problems and it has improved and modified our conventional methods of study by the knowledge gained through its use.

Its application to acquired heart disease is somewhat more limited and it finds its greatest usefulness in problems which resist solution by conventional means, and in which its particular ability to delineate certain structures is of great value, such as aneurysm, aortic disease, pericardial disease and occult heart failure. It is also valuable in evaluating mitral valve disease.

The present trend in the development of equipment is toward high speed serial radiography with the ability to make from two to 12 exposures per second, and also toward cineradiographic devices capable of up to 32 frames per second. These high speed serial technics will undoubtedly extend the field of usefulness of this method, and will amplify our current knowledge.

RESUMEN

La angiocardiografía, método de observación por contraste del corazón y de los vasos mayores, tiene el mayor valor en el diagnóstico de las anomalías congénitas. Es útil para determinar los defectos existentes, complementando a los otros métodos habituales de examen. Es aplicable a un número considerable de problemas vistos en la prática y en la mayoría de los casos que vienen para cirugía correctiva. Ha contribuído grandemente a la comprensión de estos problemas y ha mejorado y modificado nuestros métodos habituales.

La aplicación en la afección adquirida, es algo más limitada y esta más indicada en los problemas que no ofrecen solución por los métodos habituales tales como aneurismas, enfermedad aórtica, afección del pericardio e insuficiencia cardiaca oculta. También es útil para la afección de la mitral.

La tendencia actual de los equipos es hacia series de mayor velocidad para hacer hasta 12 exposiciones por segundo y hacia la cine-radiografía capaz de pasar 32 cuadros por segundo.

Estas series technicas de alta velocidad indudablemente extenderan el campo de utilizacion de éste método, y ampliaran nuestros actuales conocimientos.

RESUME

L'angiocardiographie, procédé de contraste pour l'examen du coeur, des poumons et des gros vaisseaux, prend son plus grand intérêt dans le diagnostic des cardiopathies congénitales. Elle est utile pour faire le bilan des anomalies existantes, complétant les procédés habituels d'investigation. Elle trouve son application dans un nombre considérable de problèmes que l'on rencontre en pratique, et dans la plupart des cas justiciables d'une intervention chirurgicale. Elle a grandement contribué à résoudre ces problèmes, elle a amélioré et modifié nos procédés conventionnels d'étude, et nous a permis d'acquérir des connaissances nouvelles.

Son application aux cardiopathies acquises est un peu plus limitée. Elle trouve son utilisation la plus importante dans les problèmes qu'on ne peut résoudre par les moyens habituels et pour lesquels il est capital de faire appel à sa possibilité de tracer les contours de certains organes. Il en est ainsi pour l'anévrysme, les affections aortiques, les péricardites et l'insuffisance cardiaque. Elle peut également être utile pour évaluer l'atteinte de la valvule mitrale.

La tendance actuelle dans le développement de l'équipement est en faveur de la radiographie rapide et en série, avec possibilité de faire de 2 à 12 poses par seconde et également en faveur de films radiocinématographiques pouvant aller jusqu'à 32 clichés par seconde. Les appareils permettant la prise de clichés en série à grande vitesse, permettent d'étendre le champ d'utilisation de cette méthode et d'augmenter nos connaissances.

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The Pulmonary Manifestations of Generalised Scleroderma (Progressive Systemic Sclerosis)*

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Introduction

Two aspects of generalised scleroderma have received much attention in recent years. Firstly, the widespread and sclerotic nature of the disease process has been embodied in the term "progressive systemic sclerosis," proposed by Goetz[1] in 1945, and since adopted by other authors. Secondly, connective tissue alterations are now regarded as an integral part of this entity which answers all the criteria of a grave collagen disturbance.

The purpose of this paper is to re-examine the known and possible pulmonary manifestations of systemic sclerosis, as the disease will here be termed, with reference to these newer concepts. Pleural and vascular involvement in allied collagen disorders (e.g. disseminated lupus erythematosus) are well established. The possibility of similar lesions in systemic sclerosis is therefore raised.

Hypertension in the pulmonary circuit, an entity which has recently received wide attention, is known to result from both pulmonary fibrosis and pulmonary arteritis. Systemic sclerosis is an established cause of the former, and full evidence of pulmonary vascular involvement will be presented. The relationship between systemic sclerosis and pulmonary hypertension will accordingly be examined and amplified.

The pulmonary manifestations of systemic sclerosis to be discussed in this paper are:

Tissue affected	*Pathological process*
1. Pleura.	Pleural effusion and fibrosis.
2. Broncho-pulmonary tree.	(a) Pulmosclerosis.
3. Pulmonary vascular bed.	(b) Secondary infection, and "spill-over" following esophageal lesions.
	Pulmonary hypertension due to:
	1. Anoxia (pulmosclerosis).
	2. Obstruction (sclerodermatous endarteritis).

Material

The material comprises 12 consecutive cases of systemic sclerosis which presented at Groote Schuur Hospital, Cape Town, during the period 1943-1953. Four of these came to necropsy. These cases include three of Goetz's patients previously reported.[1]

Case 1 is fully presented elsewhere by Schrire and co-workers.[2] The patients were studied by personal examination of clinical protocols,

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radiological and necropsy specimens, and clinical observation wherever possible.

Pleural Effusion and Fibrosis

None of the present group of patients had signs of pleural involvement during life. Dense pleural fibrosis was found in one case at necropsy.

A search of the literature has revealed only three cases with clinical evidence of pleural involvement in systemic sclerosis. Duffy and Bardsley report a unilateral pleural effusion. Yardumian and Kleinerman found bilateral basal dullness revealed as hydrothorax at necropsy. Necropsy confirmed a roentgenogram diagnosis in a patient of Hurly et al.

Post-mortem, evidence of pleural fibrosis has been found in five necropsies.[3, 4] Pleural lesions, whether fibrous or exudative in nature, are thus a rare complication of systemic sclerosis. Fibrosis, when it occurs, is an insidious process, not preceded by symptoms of acute pleurisy (a common feature of disseminated lupus erythematosus). Moreover, the effusions observed clinically in the few cases were not conclusively related to the sclerodermatous process itself.

Pulmosclerosis

Historical Background. Findlay (1891) was the first to remark on the association between pulmonary fibrosis and generalized scleroderma. Two of the 24 necropsy cases reviewed by Lewin and Heller (1895) had macroscopic and microscopic evidence of fibrosis, the radiological recognition of which fell to Murphy and his co-workers half a century later.[5]

In 1945, Pugh ascribed a characteristic radiological appearance to this type of fibrosis, stating that x-ray diagnosis could be made in the absence of clinical data. In the same year Getzowa also gave the first detailed pathological description. She found that lysis of alveolar walls with cystic lesions could occur in addition to the usual "compact" fibrosis. With Dostrovsky,[6] she used the term "pulmosclerosis" to denote progressive systemic sclerosis affecting the pulmonary interstitial tissue. The two types of pathological lesions were called "pulmosclerosis cystica" and "pulmosclerosis compacta" according to their nature.

Hayman and Hunt[7] (1952) collected 27 cases of pulmonary fibrosis, in generalised scleroderma recognised radiologically, adding one of their own. Since then Harper has mentioned another case, bringing the total in the English literature to 29. Towards the end of 1952 Deenstra and Jansen of Holland published six cases while the Polish investigators Chodyn and Smigielski[8] reported two. The diagnosis of pulmosclerosis is therefore still relatively infrequent.

Case 1: A colored (mulatto) male of 50 was admitted to hospital in May, 1952. For 15 years he had been coughing severely with the production of large quantities of mucoid sputum. Eight years prior to admission the first symptom suggestive of systemic sclerosis appeared—Raynaud's phenomenon affecting the fingers and toes. Ulceration and calcinosis of the fingers with increased skin pigmentation developed simultaneously. Dyspnea on exertion, of three years' duration, was not accompanied by paroxysmal nocturnal dyspnea. Actual sclerosis of the skin (cutaneous scleroderma) was only manifested one year before admission. This had involved the fingers to give typical sclerodactyly.

Examination revealed few respiratory signs. Excursions were poor but equal, with scattered crepitations on auscultation.

TABLE I
Twelve Cases of Pulmosclerosis: Nine Selected from Literature, Three from This Series

Reported by	*Cough*	*Dyspnea*	*Sputum*	*X-ray pulmosclerosis*	*Necropsy pulmosclerosis*	*Comment*
Altschule et al.[11]	yes	yes	—	yes	—	impaired pulmonary function preceded x-ray fibrosis
Bevans[12]	no	mild	no	no	gross	anatomical findings out of all proportion to clinical signs
Dostrovsky[4]	yes	chronic bronchitis		network of cavities	cystic pulmosclerosis	cystic lesions resembled tuberculosis on x-ray
Kanee[13]	—	—	—	moderate sclerosis	—	soft tissue changes may obscure x-ray fibrosis
Spain and Thomas[1]	yes	yes	much mucoid	yes	cystic and compact lesions	intercurrent infection cause of cough and sputum
Weiss et al.[14] Case 1	yes	cardiac dyspnea	—	no	focal fibrosis	necropsies revealed evidence of pulmosclerosis not detected clinically
Weiss et al. Case 2	yes	yes	yes	no	yes	
Wigley et al.[15]	—	yes	—	yes	—	i. pulmosclerosis preceded cutaneous scleroderma ii. x-ray picture resembled pneumoconiosis
Wuerthele-Caspe et al.[16]	yes	—	yes	yes	—	reported finding of "sclerobacillus"
Present series: Case 1 (Schrire[2])	yes	yes	much mucoid	yes	gross compact pulmosclerosis	pulmonary manifestations antedated sclerodactyly by fourteen years
Case 2	no	no	no	yes	—	x-ray lesion in absence of symptoms
Case 3 (Goetz[1])	yes	yes due to heart involvement	yes	no	yes	necropsy revealed pulmosclerosis not detected otherwise

The sign — denotes absence of data

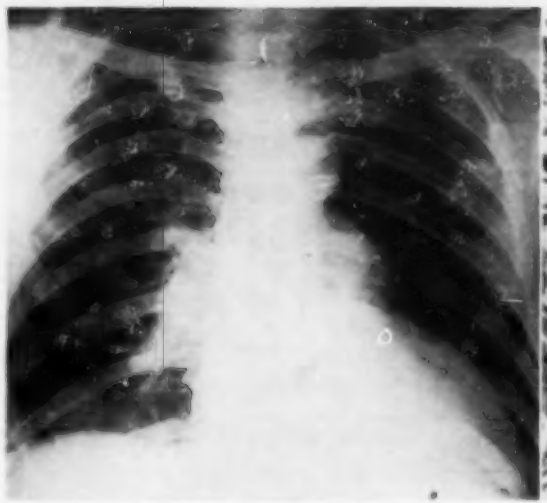

FIGURE 1

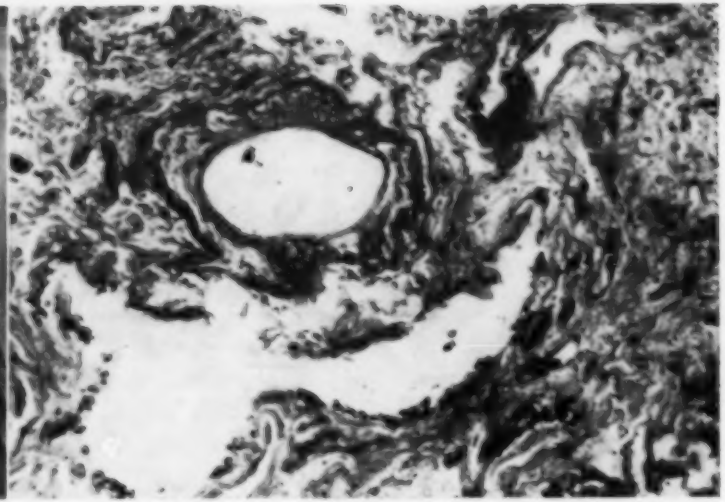

FIGURE 2

Figure 1 (CASE 1): The pulmonary artery and primary and secondary branches are usually prominent. The diffuse mottled shadows, more marked at the right base, suggest compact pulmosclerosis. There is also cardiomegaly.—*Figure 2* (CASE 1): Lung Section: gross compact pulmosclerosis but no vascular changes. Stain: V. Gieson. Magnification: 450X.

Repeated sputum examinations for M. tuberculosis were negative. For the rest the picture was that of cardiac failure, predominantly "right-sided." There was extensive edema of the legs, arms, trunk and face. X-ray films of the chest showed cardiomegaly and the changes of pulmonary hypertension (fig. 1). The pulmonary artery was prominent, and its primary secondary branches showed marked enlargement. The diffuse mottling throughout the lung fields, and more marked at the right base, suggested compact pulmosclerosis. The electrocardiogram showed the changes of right ventricular hypertrophy. Skin biopsy established cutaneous scleroderma. On cardiac catheterization an abnormally raised pulmonary arterial pressure was found. The pressure in the main pulmonary artery was 47 mm. Hg. (normal mean, 8-19 mm.[5]).

The clinical diagnosis was progressive systemic sclerosis, with pulmosclerosis and pulmonary hypertension.

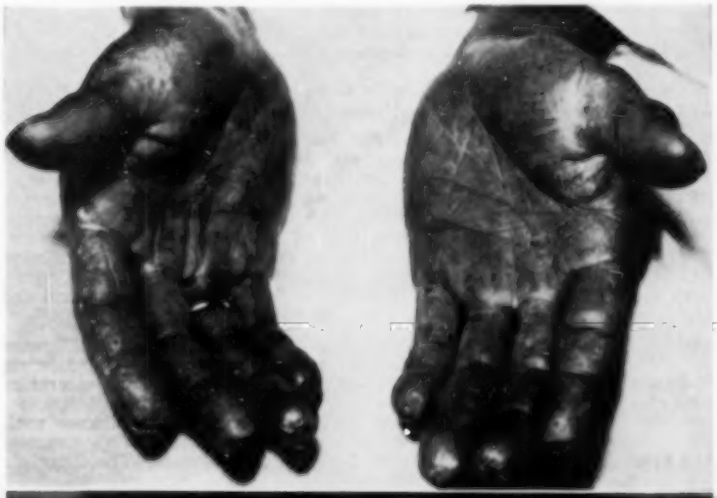

FIG. 3

FIG. 4

Figure 3 (CASE 1): Ulceration of the finger-tips in systemic sclerosis.—*Figure 4* (CASE 2): Sclerodactyly in an advanced case of systemic sclerosis. Note the shiny skin which is thickened and gives the appearance of hidebinding. The finger nails are curved but built-up nail beds of true clubbing are absent. There is an associated arthritis in this case.

The patient deteriorated and died from paralytic ileus in July, 1952.

At necropsy both lungs were bound to the chest wall by strong fibrous adhesions which obliterated the pleural cavities. The right lung weighed 655 G. (normal average: 550 G.), the left 640 G. (normal average: 450 G.). Both were extremely tough and white but not edematous. On gross section these features were attributable to severe fibrosis, apparently involving the interstitial tissue. This was most marked at the lung bases where great pressure failed to make any indentation. The mediastinal connective tissue was enormously increased, being tough, white and difficult to sever. Histologically the extreme pulmonary fibrosis was confirmed (fig. 2). The extraordinary degree of fibrosis suggested some contributary cause, but none could be found. The collagen content of the fibrous tissue stained poorly with van Gieson's stain. The acellular hyalin type of fibrosis was similar to that found in the skin. In spite of macroscopic pulmonary arterial atheromatosis, the arterioles did not show abnormal intimal or medial changes (fig. 3).

The necropsy diagnosis was progressive systemic sclerosis with cutaneous scleroderma, compact pulmosclerosis, pulmonary hypertension, pericardial and pleural fibrosis, right ventricular hypertrophy, myocardial degeneration, ascites, atrophy of the liver and leukoplakia of the esophagus.

The pulmosclerosis in this patient is reasonably viewed as the cause of his pulmonary symptoms; its presence was recognized radiologically, and established at necropsy.

Case 2: This patient, a white male born in 1904, had many stigmata of the systemic sclerosis syndrome when seen at the Out-Patients' Department in December, 1953. Raynaud's phenomenon of the hands, sclerodactyly, scleroderma of upper limbs only, and dysphagia constituted the clinical picture. At no time were there pulmonary or cardiac symptoms. Chest x-ray films revealed changes compatible with pulmosclerosis.

The generalized increase of lung markings was of scattered reticulate pattern. Sarcoidosis, although most unlikely in the full clinical context, could not be excluded on chest x-ray films alone in view of the prominent hilar shadows.

The presumptive pulmosclerosis in this patient was asymptomatic and only revealed radiologically.

Case 3: A white spinster of 44 was hospitalized with a history starting 22 years previously with Raynaud's phenomenon. Sclerodactyly had proceeded to scleroderma of the face and neck 20 years before admission. Dysphagia, calcinosis and ulceration of the ears were of 16 years duration.

There was neither clinical nor radiological evidence of any pulmonary disease until orthopnea and cyanosis preceded death with signs of bilateral bronchopneumonia. At necropsy the alveolar walls were found to be thickened and fibrosed. The diagnosis

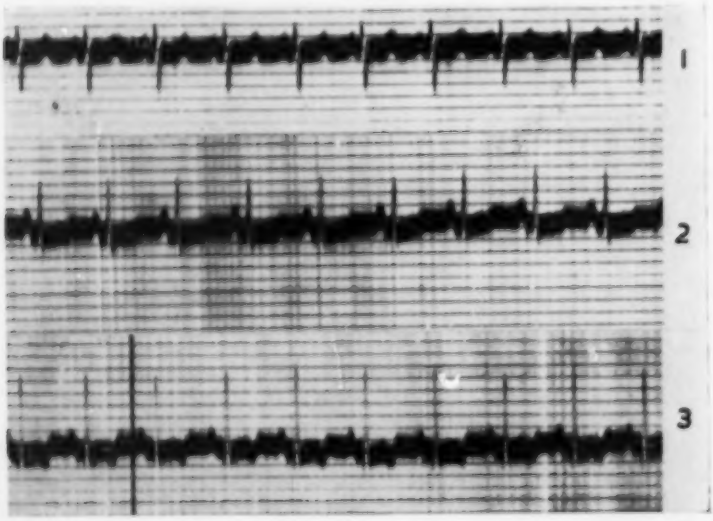

FIGURE 5 (CASE 4): Electrocardiogram shows right axis deviation with tall, spiked P-pulmonale waves in limb-lead 2.

of compact pulmosclerosis was thus made microscopically in the absence of any suggestive clinical or radiological evidence.

The Entity of Pulmosclerosis. In support of the term "progressive systemic sclerosis," Goetz[1] stressed that induration and sclerosis may occur in any organ, including the lungs, where the interstitial tissue is involved. Pulmosclerosis embodies the concept of a specific sclerotic process, progressive in nature, as a part of a widespread syndrome—systemic sclerosis.

In particular do the findings in Case 1 support the concept of pulmosclerosis, for identical histological changes were present in both skin and lung.

Comparison with Other Reported Cases. The relation of these cases to pulmonary hypertension is dealt with below; discussion is here limited to pulmosclerosis. The pertinent features are presented in tabular form and compared with those in nine other reported cases (table I). On the

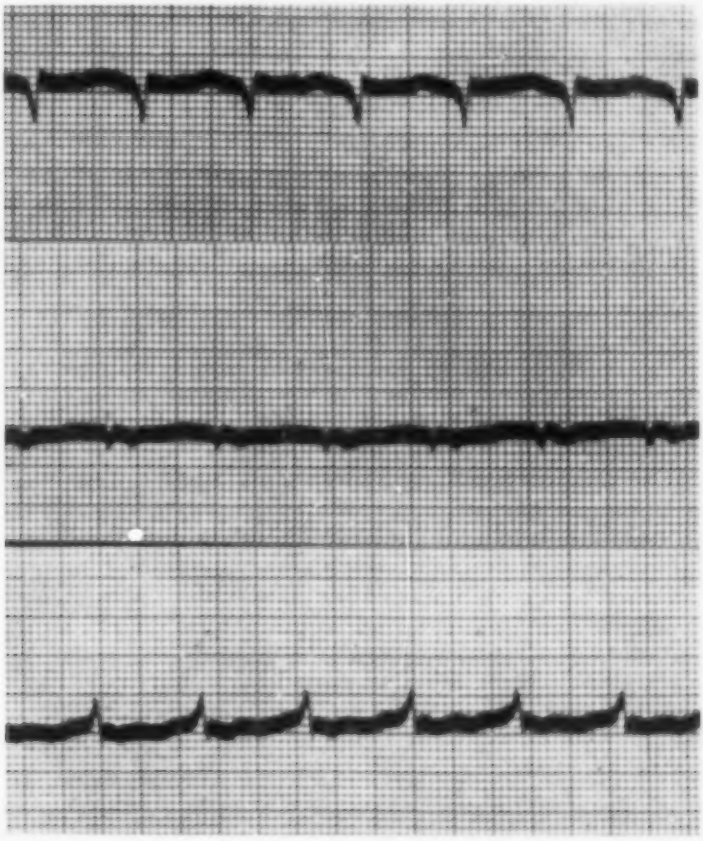

FIGURE 6 (CASE 4): Graph recorded one year after fig. 5. Right heart strain with low voltage.

basis of these data, the following points are offered in the clinical recognition of pulmosclerosis.

Time of Onset During Systemic Sclerosis. The insidious nature of the sclerotic process is revealed by the numerous necropsies showing varying degrees of histological pulmosclerosis not evident during life. This is exemplified by Case 3 of the present series.

The time of onset bears no constant relation either to the radiological evidence of pulmosclerosis or, in keeping with other visceral lesions,[10] to the external manifestations of systemic sclerosis.

Impaired pulmonary function may precede radiological evidence of pulmosclerosis.[11] On the other hand, radiological pulmosclerosis may be present without symptoms or signs[17] (as in Case 2), clinical pulmonary impairment only manifesting later.

External evidence of systemic sclerosis such as Raynaud's phenomenon, sclerodactyly, cutaneous scleroderma, calcinosis, and ulceration may all be absent when pulmosclerosis is already visible radiologically.[18] Case 1 presented with pulmonary symptoms fully seven years before Raynaud's phenomenon, ulceration and calcinosis appeared. Actual sclerodactyly and cutaneous scleroderma developed another seven years later. This stresses that finger examination in cases of obscure lung fibrosis should include attention to "numbness," "ulcer-like sores" (fig. 3), and sclerodactyly (fig. 4), in addition to clubbing. This simple clinical observation may greatly aid in the differential diagnosis of such a case.

Radiological Diagnosis of Pulmosclerosis. The description of Hayman and Hunt[7] is classic. The sclerosis starts as diffuse mottling and interlacing linear shadows confined to the lower lobes and indistinguishable from lipid pneumonia or bronchiectasis. It advances to a diffuse, netlike shadow throughout the lower two-thirds of both lung fields, more dense towards the bases and usually sparing the apices. In addition, scattered irregular mottled shadows are described. Bronchograms are usually within normal limits.

Other authors confirm this description, but of late there have been several descriptions of apical involvement,[6, 8, 9] and in some cases the pneumoconioses are closely simulated.

Involvement of the hilar, bronchial and mediastinal lymph nodes, so frequently found in sarcoidosis, has not been reported in cases described in the literature. However, prominent hilar shadows which closely resembled adenopathy were present in Case 2.

When cystic changes occur, they may be advanced enough to be visible on x-ray film, and may resemble tuberculosis.[6] In other cases the radiological appearance is a diffuse mottling, indistinguishable from that found in compact pulmosclerosis. Tomography, however, reveals the cystic character of the change. Cystic pulmosclerosis is yet another cause of "honeycombing" of the lungs.

X-ray appearances in Cases 1 and 2 could not be considered pathognomonic of pulmosclerosis. In view of this and the numerous other conditions such as idiopathic pulmonary fibrosis, radiation fibrosis, chronic asthma,

pneumoconioses, periarteritis nodosa, miliary tuberculosis, beryllosis, degenerative vascular lesions, lymphatic carcinomatous spread, pancreatic achylia, lymphomas and sarcoidosis which may all radiologically simulate pulmosclerosis at some stage, it is difficult to agree with Pugh who states that the diagnosis of pulmosclerosis may be made by x-ray film alone. Pulmosclerosis is but one cause of diffuse x-ray mottling. If such mottling be found in a patient with systemic sclerosis, the presumptive diagnosis of pulmosclerosis may be made.

Secondary Infection and "Spill-Over" Lesions

Respiratory reserve and function may be limited even in the absence of pulmosclerosis by purely mechanical factors such as sclerosis in the overlying skin, calcinosis of the soft tissues,[13] fibrous pleurisy and mediastinitis (Case 1), and the passive congestion consequent on scleroderma heart disease. Adding the hazards of dysphagia, one would expect bronchopulmonary infection to be a major mechanism of death in systemic sclerosis. Three of the five patients who died in this series suffered from terminal secondary infection. It is concluded that this may well be a frequent and formidable complication of advanced systemic sclerosis.

Complications secondary to the esophageal changes (ulceration and dilatation[1]) have been noted twice. In Harper's patient the "spill-over" from an extensively affected esophagus caused recurrent pneumonic episodes. The x-ray film of Steiner's patient showed both multiple peribronchial miliary-sized foci and a left lower lobe abscess, also attributable to "spill-over" from an atonic esophagus.

Pulmonary Hypertension

Historical Background. Pulmonary hypertension in certain clinical states was inferred by Moschowitz who first propounded the concept in 1927. The term then lapsed into obscurity and for many years was kept alive only by pathological reports such as those of Parker and Weiss and Gilmour and Evans. East revived the clinical concept in 1940, and it was a short step from Cournard and Ranges's introduction of cardiac catheterisation in man, to actual measurement of the pulmonary arterial pressure.

McMichael[20] gave the two chief causes of pulmonary hypertension of pulmonic origin as:

(a) obstruction of pulmonary vessels;

(b) anoxia associated with chronic lung disease.

In systemic sclerosis there are thus two possible causes for the development of pulmonary hypertension. Anoxia from pulmosclerosis offers one explanation. Vascular obstruction is the other main cause of pulmonary hypertension. Although Brenner (1935) did not mention systemic sclerosis as a cause of disease of the pulmonary arteries, yet Notthafft[21] had described marked sclerodermatous thickening of the pulmonary arteries in 1898. Kraus[22] (1924) found chiefly endarteritis. Similar findings are reported by other workers.[1, 3, 4, 5, 7, 13, 14]

That the two mechanisms may operate individually is illustrated by two cases of the present series.

Case 1: In this case, described above, the ante-mortem diagnosis of pulmonary hypertension was confirmed at necropsy. The minimal endarteritis and gross pulmosclerosis (fig. 2) suggest anoxia as the causal factor.

Case 4: A white spinster of 51 was admitted to hospital as a "black cardiac."

For 37 years she had been suffering from Raynaud's phenomenon of the fingers and toes. For the last 19 years dysphagia had gradually been increasing in severity. Fifteen years prior to admission the skin over the fingers hardened with resultant tapering (sclerodactyly). The sclerosis of the skin spread upwards to involve the upper arms and chest. One year before admission a new series of symptoms arose. Breathlessness on exertion and excitement was accompanied by cyanosis and swollen ankles. The cyanosis developed to such an extent that the patient described herself as "completely black." This was more marked on lying down.

On examination a few basal crepitations and rhonchi were heard. The venous pressure was raised—15 cm. above the sternal angle. Blood pressure: 110/90 mm. Hg. There was an apical triple rhythm. The liver was enlarged. Urinalysis showed a trace of albumin. Blood values were: Hb: 97 per cent, R.B.C.: 5 million, W.B.C. 12,000. X-ray films of the chest showed the heart and especially the right atrium to be enlarged. The large pulmonary artery with unusually prominent left and right main branches was associated with peripheral oligemia. Electrocardiograms taken a year previously (fig. 5) had shown right axis deviation with tall sharp P waves in lead 2 (P pulmonale). This had progressed to right heart strain with low voltage at the present admission (fig. 6). Kymography showed blunting of the cardiac excursions. The Wassermann reaction was negative. The clinical diagnosis was progressive systemic sclerosis producing Ayerza's syndrome.

Death in predominantly "right-sided" cardiac failure occurred two weeks after admission.

At necropsy the lungs showed no macroscopic abnormality. Microscopically there was no pulmosclerosis. Changes in the arterioles were striking (fig. 7). The medial hypertrophy and intimal endarteritis obliterans closely resembled the changes caused by systemic hypertension in the systemic arterioles. Visceral vessels showed similar changes. The endarteritis was especially marked in the nepatic arterioles. The heart showed right atrial dilatation and right ventricular hypertrophy. There were no abnormalities in the valves or coronary arteries, and no congenital defects. Histologically there was myocardial degeneration equally affecting both sides of the heart.

The necropsy diagnosis was progressive systemic sclerosis with cutaneous sclero-

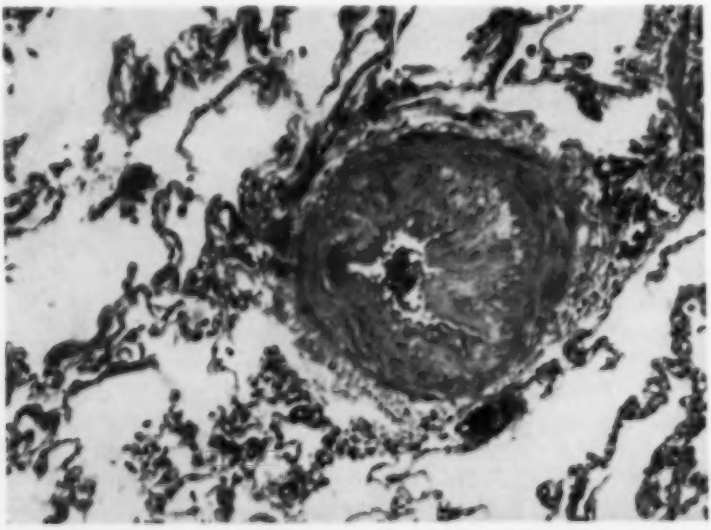

FIGURE 7 (CASE 4): Lung Section: marked endarteritis obliterans in the absence of pulmosclerosis. Stain: H. and E. Magnification: 450X.

derma, pulmonary endarteritis obliterans in the absence of pulmosclerosis, chronic cor pulmonale and "right-sided" cardiac failure.

Comment on Cases 1 and 4. Case 1 illustrates the clinical pattern described by Brill. For a varying length of time the "pulmonary phase" dominated, merging imperceptibly into the "cardiac phase."

Case 4, on the other hand, had no pulmonary phase and showed similarity to "primary" pulmonary hypertension. The chief difference is that the arteriolar changes associated with "primary" hypertension are of unknown etiology, if present, whereas the endarteritis in Case 4 was sclerodermatous in origin. (Similar vascular changes were found in other organs—as well as in the three other necropsy cases in this series.) The intense cyanosis is reminiscent of the "cardiacos nigros" of Ayerza. In a thorough review of the subject, Leopold[23] ascribes such cyanosis to a combination of pulmonary parenchymatous pathology and polycythemia, neither of which were present in this case. Clinically, the cause of this cyanosis was considered to be a right-to-left shunt through a patent foramen ovale, caused by right atrial hypertrophy in severe pulmonary hypertension. This possibility was excluded at necropsy. Similar cyanosis has rarely been found in association with endarteritis resulting from pulmonary sarcoidosis. Progressive fibrosis and cor pulmonale are other pulmonary manifestations of sarcoidosis resembling systemic sclerosis. The arteritis of sarcoidosis is not, however, an entity per se, but is consequent on involvement of the pulmonary vascular bed by granulation tissue.

Criteria for Diagnosis of Pulmonary Hypertension. The most recent upper limits of normal pulmonary arterial pressure are those of Fowler[9]—29/13 mm. Hg. Although exact diagnosis of pulmonary hypertension can only be obtained by cardiac catheterisation, careful correlation of clinical findings with pressure data has resulted in a much more confident bedside diagnosis.

In severe pulmonary hypertension some or all of the following signs suggest the diagnosis. The reduced cardiac output causes a small peripheral pulse and cold extremities. There is usually a giant 'a' wave in the jugular pulse due to right atrial hypertrophy. A striking left parasternal lift due to right ventricular hypertrophy will be noted on palpation.

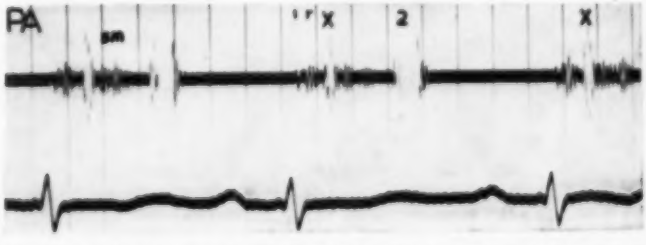

FIGURE 8: The pulmonary early systolic click (X), best heard in the pulmonary area (PA) and associated with a closely split and much accentuated second sound (2). A reduplicated first sound (lr) precedes the systolic click (X) which is followed by a pulmonary systolic murmur (sm). From a case "primary" pulmonary hypertension.

TABLE II
Pulmonary Hypertension in Systemic Sclerosis: Analysis of Literature and Two Cases From This Series

Reported by	*Clinical*	*X-Ray*	*E.C.G.*	*Necropsy*			*Likelihood of pulmonary hypertension*
				pulmo-sclerosis	*arteritis*	*heart*	
Chondyn and Smigielski Case 1[5]	P_2 loud	compact sclerosis	right axis deviation	—	—	—	likely
Chodyn and Smigielski Case 2	P_2 loud	compact sclerosis	right axis deviation	—	—	—	likely
Dostrovsky Case 1[6]	—	cystic sclerosis	—	compact & cystic lesions	occlusion sufficient to impair circulation	enlarged as result of impaired pulmonary circulation	likely
Humphreys	—	—	right axis deviation developed	diffuse fibrosis	—	cor pulmonale configu-ration	likely
Kanee[10]	—	moderate fibrosis	right axis deviation	—	—	—	doubtful
Kerley[11]	—	pulmonary arteries enlarged; peripheral oligemia; heart of "cor pulmonale" type	—	—	—	—	likely
Kraus[12]	—	—	—	diffuse fibrosis	marked endarteritis	some right-sided enlargement	possible

Linenthal and Talkov[19] Case 2	right-sided heart failure	prominent hilar markings; pulmonary "conus" enlarged	—	—	—	—	possible
McMichael[20]	death in right-sided failure	extensive diffuse fibrosis	right axis deviation	—	—	—	likely
Matsui[3] Case 1	P_2 loud	—	—	present	endarteritis	right heart and pulmonary artery dilated	likely
Matsui Case 2	—	—	—	present	endarteritis	right heart grossly hypertrophied and dilated	likely
Matsui Case 3	—	—	—	—	—	right heart & pulmonary artery dilated	doubtful
Matsui Case 4	P_2 grossly accentuated	—	—	present	endarteritis	right heart enlarged	likely
Murphy[5]	P_2 loud	fibrosis	—	extensive fibrosis	endarteritis	—	doubtful
Notthafft[21]	P_2 loud	—	—	present	media greatly thickened	right heart enlarged	likely
Spain and Thomas[4]	—	pulmonary arteries prominent; fibrosis	change from left to right axis deviation	present	moderate	right heart enlarged	case proven by cardiac catheterization
Present series: Case 1 (Schrire[9])	right-sided heart failure	pulmonary arteries prominent; fibrosis	marked right ventricular hypertrophy	gross sclerosis	normal arterioles	right ventricular hypertrophy	case proven by cardiac catheterization
Case 4 (Goetz)	right-sided heart failure; black cardiac	pulmonary arteries prominent; peripheral oligemia	right axis deviation right heart strain	absent	gross endarteritis obliterans	right ventricular hypertrophy	pulmonary hypertension virtually certain

The — sign denotes absence of data

Auscultation reveals an accentuated pulmonary second sound and recently Leatham and Vogelpoel[24] have described an added click-like sound occurring in early systole and best heard in the second and third left intercostal spaces. This they term the pulmonary early systolic click (fig. 8). In a series of 50 patients with this sign, 44 had pulmonary hypertension.

In the presence of emphysema the clinical diagnosis is much more difficult and can often only be inferred when a triple rhythm and "right-sided" failure supervene.

Electrocardiographic right ventricular hypertrophy and pulmonary hypertension have been correlated by Johnson and Taquini and their coworkers. Zuckerman and his colleagues believe that a diagnosis of chronic cor pulmonale is often arrived at by electrocardiography in the absence of definite clinical findings. Furthermore, the "P pulmonale" is closely related to pulmonary hypertension.

The radiological changes of pulmonary hypertension are due to obstruction to the blood-flow at the level of the smaller arteries and arterioles. This results in enlargement of the pulmonary artery and its left and right main branches, in contrast to the peripheral oligemia. The degree of such changes is in close relationship to the actual pulmonary artery pressure.

The diagnosis of pulmonary hypertension in a patient with systemic sclerosis requires careful clinical, electrocardiographic and radiological examination for the features described above. When pulmonary hypertension is an early event the classical signs should be found readily. However, in advanced systemic sclerosis the signs may well be obscured when the disease has extended to involve the neck and chest wall. Thus the giant 'a' wave and left parasternal lift may be hidden, while a small peripheral pulse and cold extremities are common due to the same factors that cause Raynaud's phenomenon. The diagnosis will then largely depend on the auscultatory findings, electrocardiogram and x-ray film. In Cases 1 and 4, the first clues to the development of pulmonary hypertension were, in fact, x-ray films and electrocardiographic findings.

Incidence of Pulmonary Hypertension in Systemic Sclerosis. Applying the above criteria, and also necropsy evidence of chronic cor pulmonale, 16 cases of pulmonary hypertension have been culled from the world literature and two added (table II). Of the cases in the literature, one is confirmed by catheterisation, 10 are likely, two possible and three rather doubtful. In no case except that of Spain and Thomas[4] is pulmonary hypertension specifically mentioned. Most authors overlooked findings now known to be significant. While it is apparent that pulmonary hypertension is by no means a rare complication of systemic sclerosis, it is difficult to judge the frequency of pulmonary hypertension with accuracy in view of the fact that its signs and their significance have been appreciated fully only in recent years. It is to be anticipated that greater regard to the signs of pulmonary hypertension will establish its association with systemic sclerosis more firmly. Nevertheless, on present evidence, pulmosclerosis

would appear to be a more frequent manifestation of systemic sclerosis than pulmonary hypertension.

SUMMARY

Attention is focused on the various pulmonary manifestations of generalised scleroderma (progressive systemic sclerosis). These were investigated in a series of 12 patients suffering from this condition.

Pleural involvement is uncommon in systemic sclerosis, in contrast to its frequency in other collagen diseases.

Pulmonary fibrosis due to systemic sclerosis, although a specific lesion, has no pathognomonic radiological appearance. Three illustrative cases are presented, in one of which sarcoidosis was closely simulated. The true cause of the radiological alterations may be established by giving attention to other stigmata of systemic sclerosis. The value of examination of the fingers for Raynaud's phenomenon, calcinosis, ulceration and sclerodactyly is stressed.

Secondary broncho-pulmonary infection, a frequent complication of systemic sclerosis, may be favoured by several different factors which are listed.

Pulmonary hypertension may be caused either by pulmosclerosis or sclerodermatous endarteritis. Cases are presented to illustrate these two mechanisms.

ACKNOWLEDGMENTS

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RESUMEN

Se enfoca la atención hacia varias manifestaciones pulmonares del escleroderma (esclerosis progresiva generalizada). Estas fueron investigadas en 12 enfermos con el padecimiento.

El compromiso pleural no es común en la esclerosis generalizada en contraste con su frecuencia en otras enfermedades del colágeno.

La fibrosis pulmonar debida a esclerosis generalizada, aunque es una lesión específica, no tiene aspectos radiológicos patognomónicos. Se presentan tres casos demostrativos en uno de los cuales la sarcoidosis fué simulada muy estrechamente. La verdadera causa de las alteraciones radiológicas puede ser establecida prestando atención a otrosestigmas de la esclerosis generalizada.

El valor del examen de los dedos para descubrir el fenómenode Raynaud, la calcinosis, ulceración y esclerodactilia, son recalcados. La infección broncopulmonar secundaria, una complicación frecuente de la esclerosis generalizada puede ser favorecida por los factores que se enumeran.

La hipertensión pulmonar puede ser causada ya sea por neumonoesclerosis o por endarteritis esclerodermatosa. Se presentan casos que ilustran estos dos mecanismos.

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The Diagnostic Problem of Peripheral Pulmonary Lesions*

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Much emphasis has been placed on early diagnosis and treatment of bronchogenic neoplasms. The responsibility for delays preceding definitive therapy lies with both the patient and the physician. Current campaigns directed at the public cite danger symptoms and signs of pulmonary as well as other tumors and advise early consultation with the physician. Allbritten, et al,[1] and Jewett[2] report that an average of 2.8 and 4.1 months respectively are allowed to elapse before a patient seeks the advice of a physician regarding complaints referable to the chest. Ideally, a pulmonary tumor should be detected in the asymptomatic phase. This can be accomplished by serial routine chest surveys. But Guiss[3] states that three to six months are allowed to elapse before a patient is subjected to surgery in some instances of definite primary pulmonary neoplasms discovered in a mass chest survey.

The second significant procrastination period is attributed to the physician. His contribution to the time loss averages 5 and 6.4 months respectively according to the two reports cited above.[1,2] The physician, having found a pulmonary lesion of questionable etiology, may assume an attitude of watchful waiting, or recognizing the possible serious significance, undertakes an investigation towards a precise diagnosis. The first approach is generally discredited. It is the second approach that is the concern of this paper.

No physician is desirous of subjecting the patient to thoracotomy without proper indication. Confronted then with an unexplained pulmonary infiltrate he will request additional studies, principally radiological and laboratory, hoping to achieve an exact diagnosis.

As radiologists, we were in a favorable position to observe some aspects of the intensive in-patient pre-operative work-up. Impressive was the frequency of negative results of radiological surveys, particularly in search of a primary tumor, when a lung lesion was suspected of representing a metastatic focus. It was elected to study whether x-ray and other procedures usually employed were helpful in reaching a diagnosis which might preclude surgery.

The material used for this survey included all patients who, during the past five years, were subjected to thoracotomy for resectional surgery for *peripheral* pulmonary lesions other than obvious or known tuberculosis. The pulmonary masses or infiltrations under discussion were not necessari-

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ly sharply circumscribed or nodular in appearance ("coin" lesions) on the roentgenograms. They varied in size, location, shape and sharpness of margin. Excluded was any lesion with concomitant finding of atelectasis, cavitation, lymphadenopathy, pleural effusion or thickening, or metastasis, either local to the ribs or distant. There were 78 such cases in most of which the precise nature of the lesion was reasonably in doubt prior to surgery. Fifty of them were admitted to the private service and 28 to the ward service.

Methods of Investigation and Findings

Attempts to establish a diagnosis pre-operatively were directed into the following channels:

A. *Radiography:*

The x-ray studies employed could be subdivided into two groups—thoracic and extrathoracic. There is no question regarding the necessity of intensive examination of the chest in an attempt to shed further light onto the nature of the undiagnosed infiltration. The techniques included frontal, lateral, oblique, lordotic, decubitus and Bucky views. Tomography is of particular importance for precise localization, delineation and the detection of the presence of calcium or of excavation. Occasionally this will be the only method of uncovering multiple foci of parenchymal disease and aiding in their interpretation. Bronchography and pulmonary angiography may also be employed. All other radiographic examinations are done principally in an effort to uncover a primary extrapulmonary tumor and establish the lung lesion as metastatic. In this series 28 patients were subjected to 46 extrathoracic x-ray studies. These exclaminations included pyelography (intravenous and retrograde) (22 studies); gastro-intestinal series (15 studies); barium enema (7 studies); bone survey (1 study) and cholecystogram (1 study). In no instance was a primary tumor uncovered.

B. *Sputum Studies:*

These were done in an attempt to establish tuberculosis as the etiologic basis for the pulmonary infiltrate. Thirty-four patients had repeated examinations (up to 22 per patient) for acid-fast bacilli. No positive smears or cultures were obtained. This held true even in the eight instances in which histological sections of the resected specimens showed them to be of tuberculous origin. It is of further interest that in spite of negative results, a few of the patients were placed on an extended trial of antituberculosis chemotherapy because of the strong clinical impression of tuberculosis.

C. *Bronchoscopy:*

This procedure was performed on 57 patients in an effort to visualize and biopsy the lesion. In only 12 instances was a positive diagnosis obtained. This is understandable because of the peripheral location of the mass or infiltration.

D. *Cytological Studies* (*Papanicolaou Smears*)

These were obtained either from sputa or bronchoscopic washings. Of the total of 55 bronchogenic carcinomas, 33 were subjected to such studies.

Only seven were reported as positive and six questionable. Thirteen of the non-carcinoma group were examined with 10 reported as negative and three as questionable.

A breakdown of the histological diagnoses established by surgery is as follows: bronchogenic carcinoma 55, malignant lymphoma one, bronchial adenoma three, hamartoma three, chondroma one, bronchogenic cyst one, pericardio-coelomic cyst one, granuloma (tuberculosis) 11, and organizing pneumonia (lipoid) 2. Of interest regarding the localization of these lesions was the rarity of carcinoma in the right middle lobe (only one case) and the diffuse distribution of the tuberculous lesions (right upper lobe four, right lower lobe two, right middle lobe one, left upper lobe three, left lower lobe one).

Discussion

The period of hospitalization prior to surgery varied from two days to over two months, averaging about two weeks. The elapsed time could be directly correlated with the extent of the pre-operative studies.

Routine radiological search for primary tumor on the presumption that a lung nodule represents a metastasis is generally a fruitless procedure. Certainly any leading symptom or sign such as change in bowel habits, hematuria or presence of a mass would warrant appropriate examination. The possibility of a solitary metastatic focus in the presence of a silent primary tumor is not denied. Breast, colon and kidney are reported by Minor[4] as the commonest sites of primary tumor producing pulmonary metastasis. But with the low mortality incidence for thoracotomy and pulmonary resection, as illustrated in a report by Bernatz and Clagett,[5] it would appear more feasible to establish a diagnosis by this method. Even known or definitely suspected solitary pulmonary metastatic nodules have been resected. Wood et al,[6] excised 17 metastatic lesions which represented 10.9 per cent of their total series of resected solitary circumscribed lesions. In all instances a malignant tumor had previously been removed from an organ other than the lung. Effler, et al,[7] and Wolpaw[8] each report cases with solitary metastatic carcinoma removed from the lung. In reviewing the material at this hospital, seven instances of solitary metastatic lung nodules ranging up to 7 cm. in diameter were encountered. All were from known primary extrathoracic tumors—colon two, ovary two, testis one, bone one, and cheek one. A single pulmonary focus of metastasis can justifiably be resected when it appears after a significant interval of time has elapsed following control of the primary tumor either by surgery or irradiation.

Even in the presence of a known primary tumor the discovery of a pulmonary nodule need not signify metastasis. Schafer and Scott[9] reported a patient who had a giant cell sarcoma of the wrist and who subsequently developed a nodule in the lung. On resection this was revealed to be a hamartoma. Wood, et al,[6] reported two instances in their series of circumscribed lung lesions of presumed metastatic foci in the lung which proved to be independent benign pulmonary tumors. In the first case

two separate adenocarcinomas had previously been removed from the colon. Histological diagnosis was bronchial adenoma. In the second case a carcinoma of the descending colon was detected at the same examination which disclosed a solitary lung lesion. Following removal of the adenocarcinoma of the colon, exploratory thoracotomy for presumed metastatic growth revealed a hamartoma. The possibility of a second primary malignant tumor of the lung should also be considered in such cases.

The presence of calcium in a pulmonary mass has been regarded as a reasonably certain criterion for benignity. Yet Trimble[10] reminds us that a bronchogenic carcinoma may occur in or incorporate the region of a calcified Ghon tubercle. Hodes[11] saw four patients with calcified primary nodules which, when closely followed, ultimately revealed bronchogenic carcinoma.

The presence of a not-too-well circumscribed upper lobe density would bring tuberculosis in mind and justify a short intensive search for acid-fast organisms. Age of patient, history of exposure, symptoms, and comparison with previous roentgenograms, if available, would influence decision regarding pursuit of that diagnosis. The coincidence of tuberculosis and carcinoma is reported at 1 per cent by Hedberg, et al,[12] so that even the finding of specific bacilli might lead to false security.

Bronchoscopy and Papanicolaou studies are always indicated in the presence of a central pulmonary lesion. Positive yields with peripheral foci are low. This has also been the experience of Wood, et al.[6] Negative reports do not exclude malignancy.

There is no intent here to disparage diagnostic procedures generally employed in evaluating a pulmonary lesion. A swing of the pendulum in the opposite direction, i. e., rushing a patient to surgery immediately following discovery of a lung lesion on a chest roentgenogram may result in unnecessary surgery and needless fatalities. The physician must be thorough and deliberate in his approach. Complete medical history and physical examination are fundamental. This was strikingly demonstrated recently in a patient admitted for surgery because of discovery of a mass in the left lower lobe on a routine chest survey film. Careful examination revealed the presence of a soft tissue mass in the calf of the left leg. The patient had volunteered no information regarding this, but on questioning, stated that it was there many years and not troublesome. Biopsy of the leg revealed a hemangiopericytoma. The pulmonary lesion was found on thoracotomy to be a metastatic focus.

Diagnostic procedures should be judiciously selected and expedited. An arbitrary time limit for pre-operative work-up might be set at two weeks. This may be too short a period of observation. For example, a pneumonic infiltration may persist for several weeks before starting to clear. Reports by Abeles and Ehrlich[13] and Bondi and Leites[14] emphasize the fact that, in an appreciable percentage of cases, differentiation between benign and malignant intrathoracic lesions by any current means short of any histologic examination is impossible. A more direct approach, i. e., surgical exploration, with consequent shorter hospitalization would be of consider-

able economic benefit to both patient and hospital. However, with appreciation of the varying growth potential of lung cancer, we cannot determine whether the saving of only days or a few weeks will significantly alter the ultimate prognosis of the individual patient.

SUMMARY

1. The experience at one institution with the radiological and laboratory examinations performed in conjunction with evaluation of 78 obscure peripheral pulmonary lesions, all of whom eventually came to surgery, is presented.

2. The examinations included radiography, both thoracic and extrathoracic (the latter principally a search for a primary tumor) sputum for acid-fast organisms, bronchoscopy, and cytological studies.

3. The elapsed hospital time in accomplishing these investigations averaged about two weeks.

4. Histology of surgical specimens revealed bronchogenic carcinoma in 55 of the 78 cases.

5. The endeavor of establishing a lung lesion as metastatic or of tuberculous origin was particularly unrewarding.

6. The low percentage of positive returns in the diagnostic procedures described appears outweighed by the disadvantages of delaying definitive therapy and prolongation of hospitalization.

RESUMEN

1. Se presenta en este trabajo la experiencia de una institución con exámenes radiológico y de laboratorio en cooperación para la valuación de las lesiones periféricas, obscuras, que en número de 78 más tarde llegaron a cirugía.

2. Los exámenes incluyeron radiografía tanto torácica como extratorácica (esta última en la búsqueda de un tumor primario) esputos investigando ácido-resistentes, broncoscopía y estudios citológicos.

3. El tiempo transcurrido dentro del hospital para llevar a cabo estos estudios fué por término medio de dos semanas.

4. La histología de especímene quirúrgicos reveló carcinoma bronquiogénico en 55 de los 78 casos.

La tarea de establecer si una lesión era metastática o de origen tuberculoso fué particularmente infructuosa.

6. El porcentaje bajo de resultados positivos en los procedimientos de diagnóstico descritos parece contrapesado por las desventajas de retardar un tratamiento definitivo y por la prolongación de la hospitalización.

RESUME

1. Les auteurs présentent leurs observations à l'occasion de l'examen de 78 lésions pulmonaires périphériques de nature indéterminée, mais toutes considérées comme devant être opérées. Les examens des malades comprenaient l'étude radiologique et bactériologique dans le même établissement.

2. Ces examens consistaient en radiographies à la fois thoraciques et extrathoraciques (ces dernières pour la recherche d'une tumeur primitive) bacilloscopie des crachats, bronchoscopie et examens cytologiques.

3. Le temps passé à l'Hôpital pour accomplir ces investigations était en moyenne de deux semaines.

4. L'étude histologique des pièces chirurgicales révéla un cancer bronchique dans 55 des 78 cas.

5. Les efforts dss auteurs pour établir l'origine tuberculeuse ou métastatique de la lésion pulmonaire furent couronnés de succès.

6. Le faible pourcentage des réponses positives obtenu par les procédés diagnostiques décrits ne compense pas sufisamment les inconvénients du retard apporté à la mise en oeuvre de la thérapeutique appropriée ni celui d'une hospitalisation prolongée.

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North American Blastomycosis and Bronchial Carcinoma

ALBERT ABRAHAM, M.D. and HUGH F. LUDDECKE, M.D.

Morristown, New Jersey

In our experience, fungus infections of the lungs are not common in this part of New Jersey. This case is reported because it is unusual. Among 248 autopsies performed at our hospital during the years 1952 and 1953, only three instances of pulmonary mycoses were found; this case of blastomycosis, one of aspergillosis, and a case of cryptococcosis.

The patient (D. C.) was a 70 year old colored male admitted to the Morristown Memorial Hospital on March 20, 1953. He was born in South Carolina and lived there during his early years but spent most of his adult life in New Jersey. In August, 1952, he visited in South Carolina for two weeks. He had cough and chest pain of four months duration. The family history was not contributory. The only past illness was pneumonia at the age of 10 years.

Over a period of four months prior to admission he gradually developed substernal aching associated with cough and hemorrhagic sputum. He had been smoking 20 cigarettes daily for 50 years. A physician advised him to stop smoking but symptoms continued. On the morning of hospitalization he coughed up about two ounces of bright red blood. He went to a local physician who removed one half cup of bloody fluid from the left pleural space and advised hospital admission.

On admission, examination revealed a well developed and well nourished colored male in no apparent distress. The chest was asymmetrical and over the left lower half posteriorly dullness, diminished breath sounds, and impaired tactile fremitus were elicited. The heart was normal except for a harsh systolic murmur localized to the apical area. The differential diagnosis on admission was: 1) Bronchogenic carcinoma, 2) Pulmonary tuberculosis, 3) Arteriosclerotic heart disease.

The erythrocyte sedimentation rate was 120 mm. for one hr. (Westergren). A chest x-ray film revealed prominent aortic knob, a calcific density in the right hilum and pleural effusion on the left side extending to the third anterior intercostal space.

He continued to have slight hemoptyses. On the fourth hospital day, 800 cubic centimeters of sero-sanguinous fluid was removed. Three daily sputum smears revealed no tubercle bacilli. The patient began to expectorate. For the next several days the sputum was more bloody. On the 11th hospital day, after laryngoscopy and biopsy of a mass on the right vocal cord, the pathologic diagnosis was "laryngitis, nonspecific." On the 25th day, organisms resembling blastomycetes were recovered from chest fluid obtained on the fourth hospital day, and a cell block on the same fluid revealed abnormal cells suggesting malignancy (Papanicolaou class III).

Sputum was sent to Lederle Laboratories* for further identification and the report dated August 12, 1953 was Blastomycetes Dermatitidis. "These cultures are somewhat different from the usual type in that the shift to a white, aerial mycelium is much less pronounced after several weeks incubation at 28° C. on Sabouraud's glucose agar. However, the fungal structures then formed are in agreement with the morphological descriptions on this species."

He suffered with severe anemia and intermittent hemoptysis and required six transfusions of 500 cubic centimeters of whole blood in addition to iron by mouth. Fluid was repeatedly aspirated. No malignant cells were reported but blastomycetes were again recovered. The fluid was usually chocolate-brown, and thick. On one occasion a million units of penicillin were instilled but subsequent aspiration revealed no change in quantity or quality.

On one occasion, bronchial washing stained with Papanicolaou technique were negative. A second bronchoscopic examination revealed "chronic bronchitis" and biopsy was negative for neoplasm.

A skin test with 1:1000 blastomycin on the 60th day was negative as was one with 1:500 on the 64th day. Guinea pig inoculation with the chest fluid did not produce tuberculosis.

From the Departments of Medicine (A. A.) and Pathology (H. F. L.), the Morristown Memorial Hospital, Morristown, New Jersey.

*We wish to thank Dr. Christopher H. Demos and Lederle Laboratories for assisting with the fungus identification and providing the aureomycin.

Early in the hospital course he became lethargic, anorexic and weak. His temperature ranged from 98° to 101° F.

He received aureomycin in one gram doses every six hours commencing on the 30th hospital day. Over a period of weeks he seemed to improve in that he felt better, a weight loss of five pounds was regained and the temperature slowly returned to normal.

He was able to take four grams of aureomycin a day for 57 days with only slight gastric distress and no diarrhea.

Serial x-ray films of the chest revealed a variable amount of fluid at the left base. On the 51st day there was a rounded radiolucent area in the left mid-lung field above the fluid level. This remained although the pleural effusion diminished and on the 68th hospital day a cavity with fluid level was noted at the site of the previously described density.

On the 90th day he was bronchoscoped for the third time and a friable bleeding lesion was found in the left main bronchus. He developed cardiac arrest during the procedure. Thoracotomy was performed and cardiac massage was of no avail.

Necropsy revealed about 350 ml. of yellowish-red, thick, liquid material in the left pleural space. The visceral and parietal pleural were markedly thickened and adherent with many locules containing bloody exudate. There was marked thickening of pleura in the left inter-lobar fissure and the lobes were firmly adherent. There were scattered, enlarged anthracotic nodes around the bifurcation of the trachea.

The right lung weighed 350 grams and multiple gross sections revealed no abnormality. The left lung weighed 650 grams and both lower and upper lobes were atelectatic. Upon opening the trachea and bronchi a large amount of bloody purulent material emerged, principally from the left lower main stem bronchus. In this bronchus there was marked roughening and thickening of the wall with complete obliteration of the wall architecture, and there was granular, grayish partially necrotic tumor tissue extending into the lung substance a distance of 4 centimeters. This was irregular in outline and the lung distal to this area showed numerous abscesses which contained yellowish-red or yellowish-green malodorous material. The largest of these was in association with a bronchiectatic area and this abscess was 3.5 centimeters in diameter; this was immediately distal to the tumor which formed the medial portion of its wall. The left upper lobe showed moderate atelectasis lobular consolidation and small foci of necrotic softening.

The adrenal glands appeared considerably smaller than normal and together weighed 8 grams. Cut sections showed some apparent narrowing of the cortical region. Microscopic sections of the bronchial tumor showed highly cellular squamous neoplasm with moderately intense associated desmoplastic reaction. These cells were in irregular thin and thick strands and many areas showed abundant keratin formation. Scattered epithelial pearls were found. The individual cells were large, having well defined cytoplasmic outlines. The nuclei, although variable in size, showed only moderate variation in staining. Infrequent mitoses were found.

Large areas of the tumor showed massive necrosis; only granular debris in a smudgy background being seen. The sections of the lung tissue distal to the tumor, and to a lesser extent those taken through the left upper lobe, showed an acute and chronic inflammatory process. In the latter there were many mocrophages, plasma cells and lymphocytes with some fibrosis. There was abundant necrosis in the areas of acute inflammatory reaction. No fungus organisms could be found in the many sections of the lungs.

Several bacteriologic examinations of specimens from this autopsy revealed an organism with the cultural and morphologic characteristics of North American Blastomycosis.

Anatomic Diagnosis: a) Epidermoid carcinoma of the left lower main stem bronchus, b) blastomycosis of lungs (bacteriologic report), c) bronchiectasis, d) multiple lung abscesses of left lower lobe, e) atelectasis and lobular pneumonitis, left, f) empyema, left.

Discussion

This case has been interesting and informative for several reasons. To our knowledge, this constitutes the first case of pulmonary blastomycosis seen in this part of New Jersey. We are puzzled by the negative skin tests but are reminded not to rely solely on skin sensitivity as a diagnostic method in suspected mycotic diseases. The sudden death of this patient during bronchoscopy might be related to functional exhaustion of the adrenal cortices depleted by the stress of chronic illness.

It would appear desirable to test the efficacy of aureomycin in blastomycosis alone. At the present time the only effective chemotherapy is stilbamidine and its derivatives.

SUMMARY

1. We have presented a case detailing an infection with North American Blastomycosis in the presence of a bronchogenic carcinoma.

2. It is our impression that the blastomycotic infection was favorably influenced by aureomycin; further study is necessary to determine the effectiveness of this drug.

RESUMEN

1. Hemos presentado un caso detallado de infección por blastomicosis norteamericana en presencia de carcinoma bronchogénico.

2. Tenemos la impresión de que la infección por blastomicosis, fué influenciada favorablemente por la aureomicina; se necesitan más estudios para determinar la efectividad de esta droga.

RESUME

1. Les auteurs rapportent une observation détaillée de blastomycose Nord-Américaine, coexistant avec un cancer bronchique.

2. Ils ont l'impression que l'infection blastomycotique fut influencée favorablement par l'auréomycine. Une étude ultérieure est nécessaire pour déterminer l'efficacité du produit.

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Problems in the Training of Broncho-esophagologists*

It is recognized that bronchoscopic and esophagoscopic examinations are very important methods of diagnosis in the field of diseases of the thorax. Likewise, therapeutic procedures which are important in the treatment of a variety of pulmonary and esophageal diseases can be carried out either through the instruments concerned or by the utilization of endoscopic techniques.

It follows then, that these endoscopic procedures must be carried out with such technical skill that the patient will not experience pain or undue discomfort, and in such a manner that the likelihood of any untoward effects or complications is reduced to a minimum. Not only should the endoscopist have available the optimal equipment for the performance of these examinations, but he should be conversant with the problems of thoracic and gastrointestinal diseases. He must know the indications for, and contraindications to, as well as the limitations of, the endoscopic methods.

The Committee on Broncho-esophagology has been concerned about the opportunities for training in broncho-esophagology in the United States and Canada, and also about the methods of teaching that are being employed. Hence, letters of inquiry have been sent to broncho-esophagologists in approximately 30 different medical centers, universities and clinics throughout the United States and Canada. The men queried included thoracic surgeons, otolaryngologists, internists and, in a few instances, physicians who restrict their practice to laryngology and peroral endoscopy. In all instances, the membership of the committee was personally acquainted with these men. The endoscopists to whom inquiries were sent were asked to describe the situation with respect to their specialty as it existed in their own hospitals or medical schools, and were requested to supply information regarding the facilities for training of broncho-esophagologists in the areas in which they lived.

The response to the questionnaire was almost 100 per cent. It was obvious that there is a great diversity in the manner in which the specialty of broncho-esophagology is practiced. In some cities, practically all endoscopy is done by specialists in otolaryngology; in others, by the thoracic surgeons. In a number of places there was a division of responsibility for the work in this field. In some cities the majority of the diagnostic endoscopy is done by the thoracic surgeons, whereas otolaryngologists perform endoscopy for the removal of foreign bodies or for the treatment of various diseases of the tracheobronchial tree. Otolaryngologists usually are charged with the care of esophageal strictures. We found that in some of the larger centers, the greatest share of the work is done by specialists who restrict themselves to laryngology and broncho-esophagology. Specialists in internal medicine do a limited amount of the work in broncho-

*Report of the Committee on Broncho-esophagology, American College of Chest Physicians.

esophagology. In general, specialists in medical thoracic problems are likely to restrict themselves to bronchoscopy. Esophagoscopy, on the other hand, is done by gastroenterologists in conjunction with gastroscopic work.

There is very little teaching of broncho-esophagology in the medical colleges except for a few lectures at the undergraduate level in some schools. Broncho-esophagology is almost invariably a part of the resident or fellowship type of training for thoracic surgery, but the experience is often limited. Many hospitals, clinics and medical schools still teach broncho-esophagology as part of the postgraduate training in otolaryngology, but in many localities the clinical material available to the otolaryngologist is sharply limited.

The Committee on Broncho-esophagology has concluded that the opportunities for a well-rounded training in broncho-esophagology are few. It is suggested that medical schools offer didactic lectures concerning indications for endoscopy. However, actual instruction in the techniques of bronchoscopy and esophogoscopy must be given at a graduate level. It is the feeling of the committee that too many of the physicians doing endoscopic work have inadequate training, inadequate equipment and too limited clinical material. The committee is not concerned with the primary specialty of the teacher of broncho-esophagology, so long as he is well qualified to give training in all aspects of broncho-esophagology. Not only should the student have an initial experience with animals, with models or possibly cadavers, but he should have some opportunity for the examination of persons under the supervision and scrutiny of his teacher.

The committee cannot countenance training in broncho-esophagology as given by thoracic surgeons, when the sole experience is in the field of diagnostic bronchoscopy, or by the gastroenterologists, when the experience is limited to esophagoscopy and gastroscopy. Likewise, the committee does not recommend training in this field incident to residencies in otolaryngology, with no provision for teaching in thoracic and esophageal disease.

The committee is conscious of the fact that many excellent broncho-esophagologists are being trained in various centers throughout the United States and Canada. However, it would recommend that a greater effort be made to co-ordinate the facilities for training between departments of otolaryngology, thoracic surgery, gastroenterology and medical thoracic disease in the education and instruction of young physicians who are learning broncho-esophagology. It is especially important that broncho-esophagologists have the experience and equipment necessary to minister to infants and small children. It is the belief of the committee that broncho-esophagologists should be qualified in all aspects of the field, including diagnostic bronchoscopy and esophagoscopy, the removal of foreign bodies, the dilatation of esophageal strictures and the making of bronchograms.

COMMITTEE ON BRONCHO-ESOPHAGOLOGY

Arthur M. Olsen, Rochester, Minnesota, *Chairman*

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Chevalier L. Jackson, Philadelphia, Penna.

The President's Page

At this season of the year, I wish to extend to you and your families my sincere wishes for a very enjoyable Christmas. I trust that the coming year will bring you much happiness.

To review all of the accomplishments of the College during the year 1955 would require more space than that allotted me in this issue of the journal. However, I would like to mention some of the high points which should be of interest to the members of the American College of Chest Physicians and the many readers of DISEASES OF THE CHEST.

Our 21st Annual Meeting, held in Atlantic City last June, was one of the largest and most interesting meetings of any organized by the College. Dr. Burgess L. Gordon, Chairman of the Committee on Scientific Program, and his energetic committee, presented a scientific program which was very stimulating. Among the interesting features was the first presentation of the "Fireside Conferences" in a College scientific program. These informal, unrehearsed discussions were one of the highlights of the meeting. It has been recommended to program chairmen that this popular feature be presented at future College meetings. The largest class of Fellows in the history of the College (251) was inducted at the Convocation in Atlantic City, and the Presidents' Banquet which followed, had the largest attendance of any previous banquet.

The year 1955 saw the organization of a number of excellent postgraduate courses presented throughout the country. The physicians attending these courses constituted larger enrollments than in preceding years. Much interest is shown in the postgraduate courses sponsored by the American College of Chest Physicians and the comments received from the participating physicians are most gratifying.

Chapters of the American College of Chest Physicians were organized in Hong Kong, Southern Italy, Rio Grande do Sul (Brazil), and Arkansas during the year 1955, making a total of 66 College chapters throughout the world. Many of our Fellows have traveled abroad and were impressed with the fine programs and receptions organized for them by College chapters. It is hoped that more of our Fellows will have the opportunity to lecture before our chapters in other countries during the coming year.

It is gratifying to report that 422 physicians filed applications for membership in the College during 1955. The Ninth edition of the Directory of the American College of Chest Physicians was published this year, listing 5,064 members in 86 countries and territories. The present membership of the College is 5,449.

The councils and committees which carry on the program of the College are now being completed for the coming year and it is expected that they will have interesting reports for our next annual meeting to be held in Chicago, Illinois, June 7-10, 1956.

Plans are being completed for the Fourth International Congress on Diseases of the Chest, to be held in Cologne, Germany, August 19-23, 1956, under the sponsorship of our Council on International Affairs. Those who have attended previous international congresses of the College are familiar with the many interesting features of these important international gatherings. From present indications, our Fourth International Congress promises to be even more successful and interesting than the preceding ones.

I would like to close this message by paying tribute to my predecessor, Dr. William A. Hudson, under whose capable leadership much of this progress has been made.

James H. Stygall

FOURTH INTERNATIONAL CONGRESS

Mr. Murray Kornfeld, Executive Director of the American College of Chest Physicians, met with the Governors and the Regent of the College in Germany for the purpose of completing arrangements for the Fourth International Congress on Diseases of the Chest to be held in Cologne, Germany, August 19-23, 1956.

The Congress will open on Sunday night, August 19, with a brilliant inaugural ceremony at the newly constructed Gurzenich, a beautiful, modern building in an old and historic setting. It is anticipated that the Honorable Konrad Adenauer, the Chancellor of Germany, will give the opening address. Professor Gerhard Domagk, the President of the Congress, will also speak on this auspicious occasion. The College Medal will be awarded to an outstanding scientist for meritorious achievement in the specialty of diseases of the chest. Previous recipients of the College Medal at International Congresses are: Sir Alexander Fleming, Rome, 1950; Professor Jorgen Lehmann, Rio de Janeiro, 1952; Professor Raul F. Vaccarezza, Barcelona, 1954. Dr. H. J. Moersch, President-Elect of the American College of Chest Physicians, will respond and express the appreciation of the College to the German Government for its sponsorship of this important World Congress.

The scientific program will open on Monday morning, August 20, and continue through Thursday, August 23. A symphony concert will be given Monday night, August 20, official receptions sponsored by diplomatic corps will take place Tuesday night, August 21, and the closing banquet and grand ball will be held on Wednesday night, August 22. The Congress will close at noon on Thursday, August 23. A boat trip down the historic Rhine River has been planned for Thursday afternoon.

Seated, left to right: Prof. Josef Jacobi, Hamburg, Governor for Hamburg, Schleswig-Holstein and Bremen, Secretary-General of the Congress; Prof. Joachim Hein, Toensheide/Schleswig-Holstein, Regent for Germany, Chairman of the Executive Committee for the Congress; Prof. H. W. Knipping, Cologne, Governor for Nordrhein-Westfalen, Vice-President of the Congress: Standing left to right: Prof. Rudolph Schoen, Goettingen, Governor for Neidersachsen; Prof. E. Wollheim, Wurzburg, Governor for Bavaria; Mr. Murray Kornfeld, Chicago, Executive Director; Prof. Ludwig Heilmeyer, Freiburg, Governor for Wuerttemberg-Baden

The following themes will be discussed in the scientific program: Coronary Disease; Industrial Diseases of the Chest; Tuberculosis; Pulmonary Function; Cardiac Function; and Tumors of the Mediastinum. In addition to formal presentations, a special panel of experts will be selected to discuss each of these subjects and there will be free discussion from the floor.

At the end of each daily session, Fireside Conferences will be held in the Ratskeller of the Gurzenich. These conferences will provide an opportunity for free and open discussion of many subjects, as well as for good fellowship.

Special provision will be made for the presentation of papers dealing with topics unrelated to the main themes. Motion pictures will be shown throughout the days of the Congress.

Two assembly halls will be equipped for simultaneous translation by the use of head phones. The four official languages for the Congress are German, English, French and Spanish.

Physicians planning to attend the Congress are requested to communicate with the Executive Offices, American College of Chest Physicians, 112 East Chestnut Street, Chicago 11, Illinois, U.S.A., for additional information.

Executive Sessions

The Regents, Governors, Chapter Officials and members of the Council on International Affairs of the American College of Chest Physicians will hold their opening Executive Session at the Gurzenich, Cologne, Germany, on Sunday afternoon, August 19, 1956. The closing session will be held on Thursday August 23. The host country for the Fifth International Congress on Diseases of the Chest will be announced at this meeting.

Reports will be received from College chapters throughout the world. The chairmen of the Councils on European, Pan American, Pan Pacific and African and Eastern Affairs will present resumes of College activities in their respective territories. The report of the Committee on Nominations will also be received.

All Regents, Governors, Chapter Officials and members of the Council on International Affairs of the College are requested to register in advance of the Congress for these important sessions by promptly notifying Mr. Murray Kornfeld, Executive Director, American College of Chest Physicians, 112 East Chestnut Street, Chicago 11, Illinois, U.S.A. Credentials will be prepared and forwarded to each official prior to the opening of the Congress.

Post-Convention Tour

On Friday, August 24, a special train will leave for Coblenz. The delegates and their families will proceed from Coblenz by boat, traveling up the Rhine River to Wiesbaden, arriving there Friday evening. The Mayor of the City of Wiesbaden, Dr. Mix, has planned a reception for the group and in addition a scientific program will be presented at the famous Kur Haus. It was also stated that the delegates will be admitted to their renowned Casino as guests of the city. A tour of Wiesbaden will, of course, be arranged.

On Sunday, August 26, the group will go by motor coach to Frankfurt for a brief visit and luncheon, then proceed to the University City of Heidelburg. There will be a tour of the University and a visit to the old castle. On the following day, Monday, August 27, the group will travel to Baden Baden, arriving there in time for lunch and an afternoon tour of the countryside. Dr. Schlapper, the Mayor of Baden Baden, will give a dinner for the delegates and their wives that evening, and has extended an invitation from the city to visit the Casino and special baths. A scientific session will be presented at the Kur Haus on Tuesday morning, August 28, and a special train will take the delegates to Munich that afternoon.

The mayor of Munich, Dr. Thomas Wimmer, is planning a program of entertainment for the group and a scientific session is being arranged for presentation at the Deutches Museum.

The group will travel by special train to Vienna on Tuesday afternoon, August 30, where the International Bronchoesophagological Society is holding its Congress on Friday, Saturday and Sunday, August 31-September 1-2. Information and registration for this Congress may be obtained by writing to Dr. Chevalier L. Jackson, Secretary of the Society, 3401 North Broad Street, Philadelphia, Pennsylvania, U.S.A.

During the visit to Vienna, the "City of Music," a memorable evening at the opera has been planned. A limited number of seats have been set aside for delegates who desire to attend a performance at the world famous opera house of Vienna. Tours of the city and visits to historical places will also be arranged.

International Travel Service, Inc., Palmer House, Chicago, Illinois, is the official travel agent for the Congress and for the tour. Tour folders have recently been sent to members of the College. Additional information and reservations may be obtained by writing directly to them or to the Executive Offices of the College in Chicago.

COLLEGE OFFICIALS IN GREAT BRITAIN HOLD CONFERENCE

The officers of the American College of Chest Physicians in Great Britain held a meeting in London on October 3, to discuss plans for the organization of a College Chapter in their country. At the present time there are thirty members of the College in Great Britain. It was proposed that candidates for Fellowship in the College be carefully screened by the Governors and the Regent to assure that the high standards as set forth in the College by-laws are rigidly maintained. Fellows of the College in Great Britain will participate in the Fourth International Congress on Diseases of the Chest to be held in Cologne, Germany, August 19-23, 1956.

Left to right: Sir Geoffrey Todd, Sussex, Governor for Southern England; Dr. Peter W. Edwards, Shropshire, Governor for Northern England; Dr. Richard R. Trail, London, Regent for England; Dr. Geoffrey Bourne, London, Governor for Greater London.

PAN PACIFIC CHAPTERS MEET

Dr. Chauncey C. Maher, Chicago, Illinois, was the guest speaker at a special meeting of the Japanese Chapter of the College, held on September 19 at the Kitazato Memorial Hall of the Keio University School of Medicine, in Tokyo. The meeting, arranged by Dr. Jo Ono, Regent for the College in Japan, was attended by more than 250 physicians, among whom were Dr. Alton Ochsner, New Orleans, Louisiana, and Colonel James H. Forsee of the United States Army, who were visiting in Tokyo, and Lt. Commander Hugh A. Flack of the United States Navy who is stationed in Japan. The following program was presented: The Pulmonary Cripple—Shinobu Mayamoto, Tokyo, Japan; Vectorcardiogram—Noboru Kimura, Fukuoka, Japan; The Surgical Treatment of Pulmonary Tuberculosis—Col. James H. Forsee, United States Army; Cor Pulmonale—Chauncey C. Maher, Chicago, Illinois. A dinner was given in honor of Dr. and Mrs. Maher by the members of the Japanese Chapter, attended by forty members and their guests.

Dr. Maher was the guest speaker at a special meeting of the Hong Kong and China Chapter of the College, held in Hong Kong on the evening of October 14, in the Hong Kong University Alumni Association Rooms. The meeting, arranged by Dr. Li Shu-Fan, Governor for the College in Hong Kong, and Dr. Stephen D. Sturton, Secretary-Treasurer of the chapter, was attended by members of the College and the Hong Kong Branch of the British Institute of Radiology which met jointly with the chapter. Dr. Maher lectured on "Cor Pulmonale" and Lt. Commander Flack discussed Dr. Maher's paper, with special emphasis on the treatment of cor pulmonale. A discussion period followed, during which Dr. Sturton commented on the radiological appearances of Schistomiasis, which has many features in common with cor pulmonale, referring especially to Schistosoma Japanicum in China. Dr. H. C. Ho, Government Radiological Specialist, discussed Schistosoma Mansoni and Schistosoma Haemotobium in Egypt. Dr. Y. Hans Tang, of the Hong Kong and China Chapter, spoke on Schistosoma Japanicum. A dinner, preceding the scientific program, was given in honor of Dr. and Mrs. Maher by the members of the chapter.

On October 23, Dr. Maher lectured in Honolulu before a meeting of the Hawaii Chapter of the College, held in conjunction with a meeting of the Sinclair Club, a local organization of chest specialists.

Members of the Japanese Chapter attending the meeting held for Dr. Maher.

College Chapter News

NEW YORK STATE CHAPTER

The annual clinical meeting of the New York State Chapter will be held at the Park-Sheraton Hotel, New York City, February 17-18, 1956. The following program, arranged by Dr. Ida Levine, Brooklyn, will be presented:

Friday, February 17—Morning session

9:00 a.m. Motion picture: "Principles of Respiratory Mechanics"
Jere Mead, E. P. Radford, Jr., M. B. McIlroy, B. G. Ferris, Jr., and J. L. Whittenberger, New York City
"Management of the Child with a Positive Tuberculin Test"
Margaret H. D. Smith, New York City
"Recurrent Transitory Pneumonias"
Coleman B. Rabin, New York City
"What Has Chest Surgery to Offer the Aged?"
Harvey Kugler, Glen Cove, New York
"Pulmonary Emphysema in Thoracic Surgery"
Herbert C. Maier, New York City
"Prognosis in Unresected Bronchogenic Carcinoma"
Katharine R. Boucot, Philadelphia, Pennsylvania

12:30 p.m. Luncheon
"Chronic Organizing Pneumonias"
Harold L. Israel and William J. Beckfield, Philadelphia, Pennsylvania

2:00 p.m. Afternoon session
Panel Discussion—"Stumping the Experts"
Moderator: David Spain, Brooklyn, New York
Panel: Harry L. Katz, Harold B. Lyons, Brooklyn, and Coleman R. Rabin, New York City
"The Thoracic Aorta: Lesions Amenable to Surgery"
Israel Steinberg, New York City
"Empyema in Infants and Young Children"
Charles W. Lester, New York City
"Enzymatic Treatment of Empyema Secondary to Bronchopleural Fistula"
Irving S. Shiner, Samuel A. Thompson, and Irving Innerfield, New York City

Note: Each speaker will allot the last three minutes of his time to questions from the floor.

Saturday, February 18

(This session will be held at the Tuberculosis Building of the Kings County Hospital, Clarkson Avenue near East 39th Street, Brooklyn)

Chairman: Charles E. Hamilton, Brooklyn

10:00 a.m. Small group Demonstrations:
1) Pneumoperitoneum Clinic—limited to 10 visitors
2) Total Lung Function Studies—limited to 10 visitors
3) Bronchospirometry Demonstration—limited to 5 visitors
4) Angiogram, cardiac catheterization—limited to 5 visitors
5) Unusual chest x-rays—unlimited

11:15 a.m. Combined Medical and Surgical Chest Conference

12:30 p.m. Complimentary luncheon will be served

Note: To assure a reservation for the demonstration desired, it is suggested you advise the Chapter Secretary, Dr. Harry Golembe, 10 Chestnut Street, Liberty, New York, prior to February 18.

INDIANA CHAPTER

The Indiana Chapter held its annual meeting on October 18 at French Lick Springs. The following officers were elected.

President:	H. B. Pirkle, Rockville
Vice-President	Donald W. Brodie, Indianapolis
Secretary-Treasurer:	Eva Tysse McGilvray, Rockville

VIRGINIA CHAPTER

The annual meeting of the Virginia Chapter was held in Richmond, October 16, at which time the following officers were elected:

President:	William E. Apperson, Richmond
Vice-President:	Thomas N. Hunnicutt, Jr., Newport News
Secretary-Treasurer:	Alfred L. Kruger, Norfolk

College News Notes

Dr. Anton Sattler, Fellow of the College in Vienna, Austria, arranged a conference of chest specialists at the Hotel Regina on October 18. Mr. Murray Kornfeld, Executive Director of the College who was in Vienna at the time, attended the conference and spoke on the international aspects of the College program. The following physicians attended:

Prof. Dr. Hubert Kunz	Prim. Dr. Karl Tüchler
Prof. Dr. Georg Salzer	Prim. Dr. Gerhard Berger
Doz. Dr. Anton Sattler	Dr. Emmerich Gerdenitsch
Doz. Dr. Paul Kyrle	Dr. Eduard Gabler
Dr. Alfred Fischer	Dr. Hermann Suess
Hofrat Prim. Dr. Paul Habetin	Dr. Egon Borounik
Prim. Dr. Ernst Pick	Dr. Alexander Balogh
Prim. Dr. Dlemens Lanneger	Dr. Ilse Barun-Wotke

Dr. S. J. Shane, Sidney, Nova Scotia, presented a paper on "Combined Therapy of Tuberculous Meningitis with Antimicrobial Agents and Adrenal Cortical Steroids" at the annual meeting of the Royal College of Physicians and Surgeons of Canada, held in Quebec City, recently.

Dr. William A. Hudson, Detroit, Michigan, spoke before the general practice section of the Missouri State Medical Society in Jefferson City, on October 26 and 27. Dr. Hudson spoke on "The Present Day Concept of the Treatment of Pulmonary Tuberculosis with Special Reference to Home Treatment" and "Management of Patients with Symptoms of Thoracic Disease," and also participated in the panel discussion.

At the Second Symposium on Coal Workers Pneumoconiosis, held in Elkins, West Virginia, recently, **Dr. Oscar A. Sander,** Milwaukee, Wisconsin, acted as general chairman. Guest speakers at the symposium were **Drs. Edward A. Gaensler,** Boston, Massachusetts; **J. E. Martin, Jr.,** Elkins, West Virginia; **Frank Princi,** Cincinnati, Ohio; and **David H. Waterman,** Knoxville, Tennessee.

LOS ANGELES POSTGRADUATE COURSE

The Los Angeles County Tuberculosis and Health Association has granted twenty scholarships for the Postgraduate Course on Diseases of the Chest being presented by the American College of Chest Physicians in Los Angeles, December 5-10, 1955. The registration for the postgraduate course closed at 125.

ABSTRACTS OF BARCELONA CONGRESS AVAILABLE

Many physicians who could not attend the Third International Congress on Diseases of the Chest, held in Barcelona, Spain, October 4-8, 1954, have inquired about the purchase of the attractively bound brochure prepared for the Congress.

We are pleased to announce that a limited number of these brochures, containing the abstracts of 370 papers, are available. The abstracts are printed in the five official languages of the Congress, i.e., English, French, German, Italian and Spanish. Photographs of the authors appear in most instances. The price is $5.00 postage prepaid to any part of the world and orders should be placed with Libreria Capmany, Muntaner, 363, Barcelona, Spain.

BOOK REVIEWS

THE TUBERCLE BACILLUS IN THE PULMONARY LESION OF MAN: HISTOBACTERIOLOGY AND ITS BEARING ON THE THERAPY OF PULMONARY TUBERCULOSIS. By Georges Canetti, M.D. Foreword by René J. Dubos and Walsh McDermott, M.D. Springer Publishing Company, New York, New York, 1955.

Once in every decade or era comes an outstanding new approach to perplexing scientific problems. The old well beaten pathways are left and new courses are charted. The book by Georges Canetti is one of the new approaches to an incompletely explored field of tuberculosis. In the author's words it is "a systematic study of the fate and properties of tubercle bacilli in pulmonary tuberculous lesion of man," which he has aptly called, "histo-bacteriology."

This rather modest effort of five chapters is a revised English edition of a French edition that appeared just preceding the antibiotic era. The author was aided and encouraged in preparing the English edition by René Dubos, Walsh MacDermott and others.

Never has so much been done in finding tubercle bacilli in the most important tuberculous lesions. The extent of the special work, the refinements of technical procedures and the objectivity of the discussions should place the book, for all time, high in the scale of studies devoted to the understanding of the tuberculous process in man.

The author has well realized the complexity of the problem, as well as limitations, in attempting to solve the great interplay of variables. Such factors are mentioned, as, variations of oxygen content, growth factors, virulence, the time element and blind chance as they weave in and out from patient to patient, organ to organ and site to site. "There is," he says, "a constellation of complex changing and often incomprehensible circumstances limited in space and time." In another connection he says, "The polymorphism of tuberculosis is such that extremes differ as widely as do two entirely different diseases."

In spite of the limitations, he has proceeded far into the unknown with factual data and has used rare discernment in separating fact from speculation. Although there is much discussion of possibilities, the discussions are usually pertinent and should provoke constructive thinking and action.

After a more or less perfunctory outline of the author's beliefs in pathology and pathogenesis, which follow down the middle of a rather winding road, he outlines in chapter one the commonly accepted and more or less classical basic pathology of lesions to be studied with some personal reservations. He describes briefly the tuberculous focus with its evolution into a benign type involving among many things, encapsulation, cellular metaplasia, sclerosis, calcification, and ossification and the unfavorable lesion consisting of caseation, perifocal inflammation and cavity formation.

Most of the typical lesions have been sectioned and stained for tubercle bacilli and the findings are reported in chapter two. There were few bacilli found in fibrinous lesions; in recent lesions bacilli were in proportion to the content of cellular infiltration; in older lesions there was a disappearance of bacilli as caseation formed until few or none could be found in the small older lesions; in certain caseous lesions softening takes place after which there is a marked increase in numbers of bacilli in most lesions—sometimes like a "culture of bacilli." After excavation into a cavity, the wall becomes the site of a rich growth of bacilli.

The reason for these variations has not always been determined. In the cellular content, bacilli are phagocytosed and retained until caseation appears which is a direct effect of hypersensitivity. The disappearance of growth in early caseum may be due to several factors: anoxia, exhaustion of nutrients, bacteriostatic or inhibiting substances. The increase in bacilli in *some* of the caseous lesions is enigmatic but may be due to an opening up and softening of the margins to enzymes by trauma, toxic metabolic products, to the access of oxygen and to the release of growth factors in the caseum during the softening process attributable to the penetration of secondary infections, to polymorphs, tubercle bacilli and cellular enzymes.

Chapter three embodies experimental studies of the tuberculous lesions and reviews much work on the effect of fractions of the tubercle bacillus in tissues and studies on many growth factors of the tubercle bacillus. The high point is

his own extensive study on the viability of the number of bacilli in various types of lesions. Although the disparity between the finding of acid fasts on smear and culture is wide in certain specimens, few workers will accept his use of 15 per cent sulphuric acid as a detergent, since, as he admits, it kills many bacilli. A gentler method would have given more reliable results.

In chapter four on tuberculous lesions in immunity, the author attempts to apply immune factors to the time honored host-bacillus relationship. He represents immunity as the sum total of host defensive factors which varies from species to species, individual to individual, and organ to organ. Although he has stated correctly, earlier, that caseation is a phenomenon of hypersensitivity he has not assigned the latter phenomenon any role in defense as some have done, nor does he mention Rich's work on the separation of allergy and immunity. He feels that immunity is largely a cellular problem but some humoral factors may exist. On the whole he presents little of his own work in this chapter.

In the last chapter on therapy, he reaches the highest point of present day interest and practical needs. There are four types of therapy discussed: rest, collapse, chemotherapy and resection. Resection is not considered because the therapeutic problem is removed at operation. Rest and collapse therapy, essentially the same, assist in all favorable reactions in the patient. Chemotherapy has changed in many ways, the bacterial flora of tuberculous lesions. As a result, recent exudative alveolitis and perifocal inflammation are practically wiped out. There is a collateral increase of specific cellular reaction (epithelioid cells, and atypical as well as typical giant cells). Caseous lesions, especially solid ones are affected least of all, yet there is x-ray evidence at times that clearing may take place. It seems that chemotherapy may prevent some liquefaction and the question is raised whether chemotherapy may not increase cellular reaction and fibrous tissue.

Cavities are affected most favorably as shown roentgenologically and pathologically. Some become closed out by fibrosis, some by fibrocaseous lesions, some form clean sterile cysts, others bullous cysts. There are some cavities that develop a closed bronchus enclosing inspissated pus. Finally there are those that are considered as chemotherapeutic failures where few favorable changes have resulted.

The bacteriology of lesions may be summed up as follows: there is considerable variation in the specific bacteriocidal and bacteriostatic effect of the chemotherapeutic agents, but *all act only on multiplying bacilli.* The inactive or "resting" bacilli seem to be exempt from the drugs probably in proportion to the degree of "hibernation" (reviewer's quotes). Practically all bacilli will develop resistance to drugs — individually and less so with drugs in combination. In more chronic lesions the bacilli decrease in numbers and more inactive or "resting" forms remain. Cavities having open bronchi (open lesions) nearly all contain living bacilli, but "closed lesions" contain only about one fifth (or less) as many bacilli that will grow on culture media or infect animals as appear on acid fast smears. It is not known when bacilli may have activity enough to respond to treatment and when they may be completely "at rest." It is not known when bacilli will cease to become activated so that drugs will affect them nor is there any way yet of telling when bacilli pass into permanent inactivity or death.

Prospects for the future, the author states, lie in new drugs that may have different action on resting and/or resistant bacilli and that may change the basic anatomy of the lesions by increasing cellular and fibrotic tissue.

While the work is of superior quality there are a few details besides the ones already mentioned that would have added much to value of effort. Although he does subscribe to Aschoff's classification of "primary" and "secondary lesions," there are no cases of true primary infection mentioned or shown to see what the bacillary content of such lesions may be. The "secondary lesions" he refers to are no doubt secondary to an earlier "secondary" disease process. He fails to show any example of a classical acino-nodose lesion of Aschoff which might throw some light on bacillary content during the evolution of such lesions. The same may be said of Empie's "granulie" (the gray granulation of Bayle) in contrast to the soft miliary tubercle of Laennec. While his work is confined to basic type lesions, it would be most interesting to see his method applied to the various lesions just mentioned.

In showing cavity walls he confines his work and discussion to the newly

formed cavity and does not show the findings in the old cavity with a heavy pyogenic layer and a wall of granulation tissue or one with a thick fibrous wall.

With regard to bacilli, no mention has been made of the possible effect of mutation both with regard to the resistance to drugs and the possible cause of variability of the reactivity of bacilli in the host. The innate variability of tubercle bacilli may be one of the causes of disparity in pathologic lesions.

Nobody interested in chest disease or, in fact the science of medicine, should be without this book. To those who are experienced in the laboratory sciences it is a most useful reference book and, in fact, a "congenial companion" (reviewer's quotes). To those who wish to learn more, it is a text book of high quality.

Henry C. Sweany, M.D.

ACUTE PULMONARY EDEMA. By Mark D. Altschule, M.D., Grune and Stratton, New York, 1954.

This small volume is a clear-cut critical presentation of pertinent information on the subject. Basis contribution of others are reviewed with laudable objectivity. Special credit is due to the author for his selective analysis of concepts which deal with the mechanics and etiology of this disease. Clinical manifestations are discussed in the light of Dr. Altschule's immense experience. Cardinal physiologic considerations as well as pathologic physiology are given ample space and thus serve as valuable aid to the diagnosis and treatment of acute pulmonary edema. There are a number of practical pointers in the text which qualify this book as one of the best for the daily use of the practicing physician.

Andrew L. Banyai, M.D.

RESIDENT FELLOWSHIPS

The American Trudeau Society provides a limited number of resident fellowships to promote the training of clinicians, medical teachers, and administrators in the field of tuberculosis and related pulmonary diseases. Awards are open to citizens of the United States for work within this country. Candidates should hold the degree of Doctor of Medicine and preference will be given those not more than thirty years of age.

Awards are made for graduate study in internal medicine, with emphasis on diseases of the chest, in an approved hospital. The American Board of Internal Medicine will accept one such year as part of the prerequisite training for certification in internal medicine and in pulmonary diseases.

All awards are determined by individual circumstances and are paid directly to the Fellow on a monthly basis. Fellowships are granted for one year. Not more than two renewals will be considered. Fellowship applications must be received by February 1. Appointments may begin on any date at the convenience of the applicant, who may elect the hospital in which he wishes to study and the staff member who will supervise his work.

A few fellowships at a higher level of training and award are offered to specially qualified candidates who have been assured of a continued teaching appointment upon completion of training. These fellowships are awarded for one year but may be renewed up to a total period of four years.

For further particulars, address communications to: The Director of Medical Education, American Trudeau Society, c/o The Henry Phipps Institute, Philadelphia 47, Pennsylvania.

TECHNICAL ANNOUNCEMENTS

New Antibiotic Announced by Upjohn

The discovery of a new antibiotic, Albamycin, which in preliminary clinical trials has been proved effective against a wide variety of human infections, was announced by Dr. E. Gifford Upjohn, President of The Upjohn Company.

First report of laboratory studies and clinical trials with Albamycin in humans was made by Drs. Lewis L. Coriell and Feng-Kai Lin of the Camden Municipal Hospital, Camden, New Jersey, at the Third Annual Symposium on Antibiotics, Washington, D.C., on November 4. In three children, one with a tracheotomy and bronchitis, another with a skin infection secondary to a diaper rash, and the third with a throat and lung infection, complicating whooping cough, all due to bacteria insensitive to the usual and commonly used antibiotics, "the organism disappeared promptly and the clinical symptoms subsided," the New Jersey physicians stated. They added: "These results suggest that additional laboratory and clinical studies are warranted."

Extensive clinical studies are now under way in other centers. Preliminary reports from investigators indicate that Albamycin will be effective in the treatment of bacterial infection in the skin, lungs, bone, urinary tract, and the blood stream. Thus far, Albamycin has shown no toxic effects even after three weeks of administration in large doses; no intolerance or disagreeable side effects such as diarrhea, have been noted.

Two unique and clinically significant features of Albamycin are:

1) It has shown no cross-resistance (i.e., bacteria which have become insensitive to other commonly used antibiotics remain sensitive to Albamycin).

2) It gives the highest blood levels ever experienced with any antibiotic, Dr. Upjohn said. One key to the effectiveness of an antibiotic is the amount absorbed in the blood stream where it is available to fight disease-causing bacteria. On an oral dose for dose basis, Albamycin gives blood levels 50 times higher than penicillin, 25 times higher than erythromycin, and 10 times higher than tetracycline.

New Tuberculostatic Drug "Dipasic"

Ed. Geistlich Sons Ltd., leading European chemical and pharmaceutical manufacturer, announces the appointment of The Panray Corp. of New York City, to distribute and clinically evaluate "Dipasic" (GEWO 339) in the United States.

"Dipasic" (GEWO 339) is a new tuberculostatic, offering certain advantages as compared with the conventional INH and PAS or INH and streptomycin combination therapy. Combined therapy postpones the emergence of resistance on the part of tubercle bacilli or prevents it, since several metabolic routes of the tubercle bacilli are interfered with. From this consideration, it was a short step to combining two well-tried tuberculostatics chemically, thus obtaining at least the results of "shuttle" therapy and in addition securing advantages as regards simplicity in application and compatibility. Since "Dipasic" is effective even in small doses, it is very economical, and bacteriological tests indicate that this new chemical substance is superior to a physical mixture of the two tuberculostatics INH and PAS. A special feature noticeable in "Dipasic" therapy is that, as compared with combination therapy as practiced hitherto, considerably less PAS is applied.

Initial *in vitro* studies show that "Dipasic" (GEWO 339) is not only very effective against the normal strains, but also shows complete effectiveness against various strains resistant to PAS, INH, and streptomycin. "Dipasic" is effective with all forms of tuberculosis, particularly for cases of fresh exudative pulmonary tuberculosis and as a preoperative measure.

For information concerning clinical investigations write to the Panray Corp., 340 Canal Street, New York 13, New York.

THE INDEX
TO THIS VOLUME HAS BEEN REMOVED
FROM THIS POSITION AND PLACED AT
THE BEGINNING OF THE FILM FOR
THE CONVENIENCE OF READERS.

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MEDICAL SERVICE BUREAU

Positions Available

Clinical director wanted for modern tuberculosis annex to general hospital (127 tuberculosis patients at present); must be citizen of the United States and eligible for Louisiana licensure; salary dependent upon qualifications and experience. Building program will increase capacity to over 200 beds. All modern facilities available. Write to: O. P. Daly, M.D., Superintendent, Lafayette Charity Hospital, Lafayette, Louisiana.

Staff physician wanted for Neuropsychiatric-Tuberculosis service at newly activated Veterans Administration Hospital, Sepulveda, California, located 25 miles from downtown Los Angeles. Tuberculosis experience required. Affiliated with three medical schools. Apply: Manager, VA Hospital, Sepulveda, California.

Assistant medical director wanted for 100 bed tuberculosis hospital. North American graduate, salary $8,500. complete maintenance. Apply: Medical Director & Superintendent, District Five Tuberculosis Hospital, London, Kentucky, or State Tuberculosis Hospital Commission, New State Office Building, Frankfort, Kentucky.

Medical Director wanted, North American graduate, five years tuberculosis experience, relatively new 100-bed tuberculosis hospital. Salary $10,000. Complete maintenance. Apply State Tuberculosis Hospital Commission, New State Office Building, Frankfort, Kentucky.

CALENDAR OF EVENTS

NATIONAL AND INTERNATIONAL MEETINGS

22nd Annual Meeting, American College of Chest Physicians
Hotel Sherman, Chicago, Illinois, June 7-10, 1956

Fourth International Congress on Diseases of the Chest
Council on International Affairs
American College of Chest Physicians
Cologne, Germany, August 19-23, 1956

POSTGRADUATE COURSE

9th Annual Postgraduate Course on Diseases of the Chest
Bellevue-Stratford Hotel, Philadelphia, March 19-23, 1956

CHAPTER MEETING

Clinical Meeting, New York State Chapter
New York City, February 17-18, 1956

in intractable asthma,[1-3] allergic dermatoses[2-5] and other allergic disorders

- greater therapeutic benefits
- fewer unwanted effects

METICORTELONE

METICORTELONE resembles METICORTEN in antirheumatic, anti-inflammatory and antiallergic effectiveness.[1-13] The availability of these new steroids, first discovered and introduced by Schering, provides the physician with two valuable agents for safer, more effective cortical hormone therapy.

Bibliography: (1) Henderson, E.: New developments in steroid therapy of rheumatic diseases, presented at New Jersey State Medical Society Meeting, Atlantic City, New Jersey, April 17-20, 1955. (2) Clinical Research Division, Schering Corporation: Compilation of investigative reports. (3) Criep, L. H.: Prednisolone and prednisone in the treatment of allergic diseases, to be published. (4) Robinson, H. M., Jr.: First International Conference on Meticorten and Meticortelone, New York City, May 31-June 1, 1955. (5) Sternberg, T. H., and Newcomer, V. D.: Am. Pract. & Digest Treat. *6*:1102, 1955. (6) Bunim, J. J.; Pechet, M. M., and Bollet, A. J.: J.A.M.A. *157*:311, 1955. (7) Waine, H.: Bull. Rheumat. Dis. *5*:81, 1955. (8) Tolksdorf, S., and Periman, P.: Fed. Proc. *14*:377, 1955. (9) Herzog, H. L., and others: Science *121*:176, 1955. (10) Bunim, J. J.; Black, R. L.; Bollet, A. J., and Pechet, M. M.: Ann. New York Acad. Sc. *61*:358, 1955. (11) Boland, E. W.: California Med. *82*:65, 1955; abs., Curr. M. Digest *22*:53, 1955. (12) King, J. H., and Weimer, J. R.: A.M.A. Arch. Ophth. *54*:46, 1955. (13) Gordon, D. M.: Prednisone and prednisolone in ocular disease, to be published.

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*T. M.

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